



Ministry of Health

NATIONAL **ANTIMICROBIAL** STEWARDSHIP

**GUIDELINES FOR HEALTH CARE SETTINGS
IN KENYA**

MARCH 2020



Ministry of Health

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FOREWORD

The discovery of antibiotics in the early 20th century has over time transformed health care, significantly reducing morbidity and mortality from infectious diseases and paving the way for major achievements in medicine. The increase in organisms showing resistance to commonly available antibiotics is further complicated by the slow pace of discovery and development of new antibiotics. This has rendered standard treatments ineffective and facilitated the spread of drug-resistant infections, leaving the community vulnerable. To ensure that we continue to benefit from antibiotics, practical approaches to the use of both existing and newly developed antibiotics are essential.

Following reports of alarming rates of resistance, the Global Action Plan on Antimicrobial Resistance (AMR) was adopted in 2015 by all member states at the World Health Assembly, the Food and Agriculture Organization (FAO) Governing Conference, and the World Assembly of the World Organization for Animal Health (OIE) delegates. During the United Nations (UN) general assembly high-level meeting in September 2017—the fourth time a health issue has been discussed at the assembly—the agenda on drug-resistant bacteria was presented. UN secretary general Ban Ki-moon referred to AMR as a “fundamental threat” to global health and safety that would make provision of universal health coverage (UHC) difficult or impossible if it is not quickly and comprehensively addressed. This was followed by the development of the National Policy and Action Plan (NAP) on the Prevention and Containment of Antimicrobial Resistance in Kenya in 2017.

The AMR NAP aims to: Improve awareness and understanding of AMR through effective communication, education, and training; Strengthen the knowledge and evidence base through surveillance and research;

Reduce the incidence of infection through effective sanitation, hygiene, and infection prevention measures; Optimise of the use of antimicrobial medicines in human and animal health and Develop an economic case for sustainable investment that takes into account the needs of the country and investment in new medicines, diagnostics, tools, vaccines, and other interventions. The need for establishing antimicrobial stewardship (AMS) programmes across the health care spectrum is a strategic objective in the NAP to optimise the use of antimicrobials in human and animal health. This guideline focuses on optimising the use of antimicrobials in human health through robust Medicines and Therapeutics Committees (MTCs) to ensure patient safety, optimal treatment outcomes, and reduced costs of treatment as we work toward UHC.

This guideline provides an avenue to comprehensively evaluate the wide range of interventions that can be implemented by AMS programmes in different health care settings in light of different resource capacities. It also addresses approaches to measure the success of these interventions and the structure of an AMS programme, emphasising the importance of physician and pharmacist leadership, robust microbiology capacities, infectious disease expertise, and measurement and feedback as critical components of AMS programmes. This guideline will be backed by strong government and institutional commitment and collaborative actions across the disciplines and calls on everyone to act now to avert the threat of AMR in Kenya and the world.



Sicily K. Kariuki, EGH, MBS, CBS
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PREFACE

The discovery of the first antibiotic, penicillin, in 1928 is credited to Alexander Fleming, who cautioned of an impending crisis during his Nobel Prize award ceremony in 1945. He pointed out that underdosing may expose microbes to non-lethal quantities of the drug, making them resistant. Since then, antibiotics have proven to be one of the most effective interventions in human medicine. Unfortunately, the overuse and misuse of this valuable resource has resulted in a global AMR crisis. Seven decades after Fleming's discovery, the first UN General Assembly high-level meeting on drug-resistant bacteria was convened in September 2017, the fourth time the General Assembly had held a high-level meeting to discuss a health issue. It was noted that AMR, if left unchecked, would undermine sustainable food production and hinder the achievement of the sustainable development goals.

The concept of AMS is therefore a fundamental component of the solution to the crisis. AMS will reduce overuse and misuse of antibiotics by promoting prudent use, which is vital to sustainable prevention and treatment of infectious diseases. The National Action Plan on the Prevention and Containment of AMR clearly outlines the areas of focus, which include developing and implementing stewardship guidelines, enhancing regulations, enhancing human resource capacity, ensuring access to essential antimicrobials, strengthening laboratory diagnostic capacity, and ensuring sustainable access to quality essential antimicrobials.

To support UHC, efforts must also focus on sustaining an efficient supply chain system with robust MTCs established across all levels to ensure the availability and accessibility of quality medicines to all patients at all times, with an emphasis on appropriate use by both patients and prescribers. This will ensure prudent prescribing across communities and settings, diverse patient populations, geographical regions, and resource capacity and cultures. For this to be realised, a truly innovative, practical, flexible, collaborative, and cross-disciplinary approach is required to effect true transformational change in antibiotic prescribing and utilization practices.

We welcome the timely publication of this guideline as it highlights the need to combine traditional and modern methods to successfully deliver stewardship interventions to ensure better awareness and penetration into health care systems and communities.

A handwritten signature in black ink, consisting of several overlapping loops and a long horizontal stroke extending to the right.

Dr. Rashid Aman, PhD
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Ministry of Health

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The National Antimicrobial Stewardship Guidelines for the Health Care Settings in Kenya, 2019 have been developed through the contributions of many individuals and institutions that are committed to improving antimicrobial use in hospitals and within the community and reducing the risk of harm to patients from inappropriate antimicrobial prescribing and use. The Kenyan Ministry of Health (MOH) wishes to thank the following contributing authors led by the National Technical Working Group on Antimicrobial Stewardship for their expertise and time given to the writing of these guidelines. Finally, the MOH wishes to acknowledge the technical and financial support provided by the Action on Antibiotic Resistance (ReAct) Africa / Ecumenical Pharmaceutical Network (EPN) and the American people through the United States Agency for International Development (USAID) Medicines, Technologies, and Pharmaceutical Services (MTaPS) program, contract number 7200AA18C00074.

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LIST OF ACRONYMS

| | |
|---------------|---|
| ACDC | Africa Centres for Disease Control and Prevention |
| AFENET | Africa Field Epidemiology Network |
| AMC | Antimicrobial consumption |
| AMR | Antimicrobial resistance |
| AMS | Antimicrobial stewardship |
| AMU | Antimicrobial use |
| ART | Antiretroviral therapy |
| ASLM | African Society for Laboratory Medicine |
| ASM | American Society for Microbiology |
| ASO | Automatic stop order |
| AWaRe | Access, Watch, and Reserve |
| CASIC | County Antimicrobial Stewardship Interagency Committee |
| CDC | Centers for Disease Control and Prevention |
| CDI | <i>Clostridium difficile</i> infection |
| CEO | Chief Executive Officer |
| CHA | Community health assistant |
| CHMT | County health management team |
| CHU | Community health unit |
| CHV | Community health volunteer |
| CIPCAC | County Infection Prevention and Control Committee |
| CLSI | Clinical Laboratory Standards Institute |
| CMTC | County Medicines and Therapeutics Committee |
| CP | community pharmacy |
| DCS | Director of clinical services |
| DDD | Defined daily dose |

| | |
|-----------------|--|
| DHIS2 | District Health Information Software version 2 |
| DOT | Days of therapy |
| ECSA | East Central and Southern Africa Health Committee |
| FAO | Food and Agriculture Organization |
| GHSA | Global Health Security Agenda |
| ID | Infectious disease |
| IFMIS | Integrated financial management system |
| IPC | Infection prevention and control |
| IPCC | Infection Prevention and Control Committee |
| ICT | Information and communications technology |
| IV | Intravenous |
| KEML | Kenya Essential Medicines List |
| KEMRI | Kenya Medical Research Institute |
| LIMS | Laboratory Information Management System |
| LMICs | Low- and middle-income countries |
| M&E | Monitoring and evaluation |
| MDR-TB | Multidrug-resistant tuberculosis |
| MOH | Ministry of Health |
| MRSA | Methicillin-resistant <i>Staphylococcus aureus</i> |
| MTC | Medicines and Therapeutics Committee |
| NACOSTI | National Commission for Science, Technology and Innovation |
| NAP | National action plan |
| NASIC | National Antimicrobial Stewardship Interagency Committee |
| NASIC-TC | National Antimicrobial Stewardship Interagency Committee-Technical Committee |
| NHIF | National Health Insurance Fund |

| | |
|---------------|--|
| NIPCAC | National Infection Prevention and Control Committee |
| NMTC | National Medicines and Therapeutics Committee |
| NP HLS | National Public Health Laboratory Services |
| NQCL | National Quality Control Laboratory |
| OIE | Organisation mondiale de la santé animale (World Organisation for Animal Health) |
| OTC | Over the counter |
| PBF | Performance-based financing |
| PCR | Polymerase chain reaction |
| PDSA | Plan-do-study-act |
| PO | Per oral |
| PPB | Pharmacy and Poisons Board |
| PPS | Point prevalence survey |
| QC | Quality control |
| QIT | Quality improvement team |
| STG | Standard treatment guideline |
| TB | Tuberculosis |
| TWG | Technical working group |
| UHC | Universal health coverage |
| UN | United nations |
| UTI | Urinary tract infection |
| VEN | Vital, essential, nonessential |
| WHO | World Health Organization |
| XDR-TB | Extensively drug-resistant tuberculosis |

GLOSSARY OF TERMS

Active pharmaceutical ingredients are biologically active ingredients in a drug.

Antibiogram is a periodic summary of the susceptibility patterns of local bacterial isolates to available antibiotics.

Antibiotics are medicines that kill or inhibit the growth of bacteria.

Antimicrobials are medicines that kill or inhibit the growth of a variety of microorganisms such as bacteria, fungi, or viruses.

Antimicrobial prophylaxis is the process of administering antimicrobials to prevent the development of infection.

Antimicrobial resistance is the ability of a microorganism to stop or prevent the activity of an antimicrobial that was once effective against it.

Antimicrobial use refers to the evaluation of the quantities of antimicrobials used in a specified patient group or population, and the indications for their use over a specified period of time.

Antimicrobial sensitivity testing refers to laboratory tests that are used to determine the antimicrobials that a particular microorganism or groups of organisms are susceptible to.

Antimicrobial stewardship is a coordinated programme that promotes the appropriate use of antimicrobials to improve patient outcomes, reduce antimicrobial resistance, and limit the spread of multidrug-resistant organisms.

Appropriate use of antimicrobials is the use of antimicrobials for the right condition and right patient for the right duration. It is also called responsible use.

Automatic stop order refers to the application of stop dates to antimicrobial orders when the duration of therapy is not specified to prevent unnecessary prolonged use of antimicrobials.

AWaRe categorization is the classification of antimicrobials into the Access, Watch, and Reserve categories based on their spectrum of activity, toxicity, high resistance potential, and cost.

Broad spectrum antibiotic is an antibiotic that works against a wide range of gram-positive and gram-negative bacteria.

Clinical pharmacist is an expert in the therapeutic use of medication whose role is to provide medication therapy evaluations and recommend the best treatment to patients.

Community pharmacy, also known as a retail pharmacy, is a type of pharmacy that allows the public access to medicines and advice about their health.

De-escalation refers to the reduction in the spectrum of administered antibiotics by either discontinuing or switching to an antibiotic with a narrower spectrum.

Defined daily dose is the assumed average daily dose for a drug used for its main indication. It is a measure of antimicrobial use.

Diagnostic stewardship is the coordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions.

Empiric treatment refers to the choice of antimicrobials by clinicians based on their clinical judgement and expertise in the absence of laboratory data and other information.

Hospital-acquired infection is an infection acquired during admission to a hospital and excludes any infection contracted before admission. It is also referred to as a nosocomial infection.

Inappropriate use of antimicrobials refers to use of antimicrobials where they are not indicated or for non-therapeutic reasons.

Infection prevention and control refers to interventions intended to minimise the spread of disease-causing organisms and reduce the likelihood of infection, such as hand hygiene, sterilisation and disinfection, environmental cleaning, and education.

Isolate is a microorganism obtained from a specimen such as blood or stool.

Levels of hospitals in Kenya: Level 6: national referral hospitals; level 5: provincial referral hospitals; level 4: district and sub-district hospitals; level 3: health centres; level 2: dispensaries.

Methicillin-resistant *Staphylococcus aureus* is a type of *Staphylococcus* bacteria that is resistant to methicillin and other beta lactam antibiotics.

Multidrug resistance is the resistance of microorganisms to at least one antibiotic in three or more drug classes.

National action plan is a policy document that provides a comprehensive policy framework and priority actions to contain the emergence and spread of antimicrobial resistance.

One Health is a multisectoral approach to designing and implementing programmes, policies, and research in combating antimicrobial resistance.

Over-the-counter sale of medicine refers to purchasing medicines at the pharmacy without a prescription.

Pathogens are disease-causing microorganism such as bacteria, viruses, and fungi.

Priority microbes are microbes that cause diseases that are associated with high rates of antimicrobial resistance, morbidity, mortality, and treatment costs.

Sample is a specimen collected for laboratory testing. Samples may include blood, stool, and sputum.

Supply chain is a network of individuals, organisations, activities, resources, and technologies involved in the delivery of a product from the source to the intended institutions.

Surveillance is the detection and monitoring of trends and threats in antimicrobial resistance and antimicrobial use to inform strategies that reduce the risks of antimicrobial resistance.

Universal health coverage is a health care system that provides promotive, preventive, curative, rehabilitative, and palliative services to residents of a country or region while protecting them from the financial implications of those services.

CHAPTER 1 BACKGROUND

1.1. Introduction

AMR is a serious threat to global public health that requires action across different government sectors and society. AMR refers to the ability of microbes to grow in the presence of a drug that would normally kill them or inhibit their growth. While it is a natural evolutionary phenomenon that happens as microbes adapt to naturally produced antimicrobials, the indiscriminate use of antimicrobial drugs has accelerated its progress.

AMR threatens effective treatment of infections and leads to prolonged duration of illness, higher morbidity and mortality rates, and increased cost of health care. Additionally, poor infection control, inadequate sanitary conditions, and improper food handling encourage the spread of AMR given that people, animals, food, and the environment harbour resistant microbes. Exacerbating the problem are inadequate health systems and infrastructure, which reinforce a largely empiric pattern of antimicrobial prescribing. The antimicrobial production pipeline has gone dry, with no new antimicrobials being produced and released into the market. This, coupled with the indiscriminate sale of over-the-counter (OTC) antimicrobials with minimal regulation, oversight, or quality control, further compounds AMR in Africa. AMR, which renders antimicrobials unusable, is likely to have a negative impact on the achievement of UHC.

1.2. Global burden of antimicrobial resistance

Globally, at least 700,000 people die each year of drug resistance to illnesses such as bacterial infections, malaria, HIV/AIDS, and tuberculosis (TB). Worrying trends that have been reported worldwide include the high resistance rates of *Klebsiella pneumoniae* to carbapenems, fluoroquinolone resistance in *E coli*, and resistance to

quinolones and third-generation cephalosporins in gonorrhoea, necessitating the review of gonorrhoea, syphilis, and chlamydial infection treatment guidelines by the World Health Organization (WHO).

Resistance to first-line drugs to treat infections caused by *Staphylococcus aureus*—a common cause of severe infections in health facilities and the community—is widespread, with a mortality rate of 64% being reported among people with methicillin-resistant *Staphylococcus aureus* (MRSA). Colistin is the last-resort treatment for life-threatening infections caused by Enterobacteriaceae, which are resistant to carbapenems, yet emerging resistance has been reported.

WHO estimated that, in 2014, there were about 480,000 new cases of multidrug-resistant tuberculosis (MDR-TB), a form of TB that is resistant to the two most powerful TB medicines. Only about one-quarter of these (123,000 cases) were detected and reported. MDR-TB requires treatment courses that are much longer and less effective than those for non-resistant TB. Globally, only half of MDR-TB patients were successfully treated in 2014. Among new TB cases in 2014, an estimated 3.3% were multidrug resistant. The proportion is higher among people previously treated for TB, at 20%. Extensively drug-resistant tuberculosis (XDR-TB), a form of TB that is resistant to at least four of the core TB drugs, has been identified in 105 countries. An estimated 9.7% of people with MDR-TB have XDR-TB.

Resistance to the first-line treatment for *P. falciparum* malaria (artemisinin-based combination therapy) has been confirmed in five countries of the Greater Mekong sub-region (Cambodia, the Lao People's Democratic Republic, Myanmar, Thailand and Vietnam). On the Cambodia-Thailand border, *P. falciparum* has become resistant to almost all available antimalarial medicines, making treatment more challenging. The spread of these resistant strains to other parts of the

world could pose a major public health challenge and jeopardise important recent gains in malaria control.

Resistance to antiretroviral therapy (ART) has also been reported. In 2010, an estimated 7% of people starting ART in developing countries had drug-resistant HIV, as opposed to 10 to 20% in developed countries. For those restarting treatment, higher resistance levels, ranging from 15 to 40%, have been reported. These have significant economic implications as second- and third-line regimens are three and 18 times more expensive, respectively, than first-line drugs. The WHO recommendations that everyone diagnosed with HIV starts ART will increase the use, further increasing the chances of resistance. To maximise the long-term effectiveness of first-line ART regimens, it is essential to continue monitoring resistance and minimise its further emergence and spread. To mitigate this, WHO developed a new Global Action Plan for HIV Drug Resistance (2017–2021) in consultation with partners, countries, and key stakeholders. Apart from HIV, resistance to antiviral drugs by other viruses has been documented. Influenza viruses have shown resistance to amantadine and rimantadine, while resistance to oseltamivir remains low at 1 to 2%.

1.3. Burden of antimicrobial resistance in Kenya

Sentinel studies from 2003 to 2009 show that AMR is a growing concern in Kenya. Common life-threatening pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, *Non-typhi Salmonella*, and *Neisseria gonorrhoeae* have all developed high levels of resistance to common first-line drugs such as ampicillin and co-trimoxazole. Multidrug-resistant organisms are emerging as a significant health problem in hospital settings. A study conducted in Western Kenya found that 50% of the pathogens isolated from bacterial diarrhoea were not susceptible to first-line antibiotics, and 75% were resistant to three or more agents. Notably, multidrug-resistant *non-typhi Salmonella* in hospital and community settings rose from 31% in 1993 to 42% in 2003. High prevalence of fluoroquinolone

resistance (53.2%) in *Neisseria gonorrhoeae* isolates was demonstrated from four clinics in three regions of Kenya between 2009 and 2010.

1.4. Antimicrobial use patterns in Kenya

In Kenya, the first comprehensive situation analysis on trends in antimicrobial use (AMU) and AMR was published in 2011 for livestock and human medicines, with an update in 2016. However, data on AMU in agriculture, including fisheries and plant health, were unavailable. It was observed that in some regions of the country there was evident overuse and abuse of antimicrobials, yet paradoxically some communities were unable to access these vital lifesaving medicines.

Cross-sectional studies and point prevalence surveys (PPS) have been conducted in hospitals across the country, and they reflect a high prevalence of antibiotic use (45–69%); irrational antibiotic prescription across wards, especially with regard to third-generation cephalosporins and extended-spectrum penicillins; and limited or no use of culture and sensitivity tests to guide therapy. Paediatric and surgical wards have been flagged as areas of AMS focus. Findings from a yet-to-be-published multicentre PPS targeting three large public hospitals between September 2017 and April 2018 mirror these results, with a prevalence of 46%. This espouses the need to develop and implement AMS guidelines for the country. At the community pharmacy level, a study indicated prudent use of antimicrobials at pharmacies superintended by pharmacists.

Antimicrobial use and resistance data from public health facilities have been collected on a large scale by a national data site, the District Health Information Software version 2 (DHIS2). This accounts for only 50% of health care institutions in the country. There is a paucity of antimicrobial usage and resistance data from import and manufacturing sites, hospitals, community pharmacies, research facilities, institutions of higher learning, and veterinaries because a consolidated national data collection method for end-point AMU is lacking.

1.5. National policy and action plan for antimicrobial resistance

Following the endorsement of the Global Action Plan on AMR at the 68th World Health Assembly, member states were required to develop their NAPs in response to the growing threat of AMR. A situation analysis was conducted in Kenya in 2011, and the results subsequently guided the development of a National Policy and Action plan on the prevention and containment of AMR in Kenya in 2016.

The NAP on Prevention and Containment of Antimicrobial Resistance 2017–2022 provides a common framework for action by all stakeholders in Kenya. These stakeholders are drawn from different sectors, including human health, animal health, agriculture, fisheries, and environmental sectors, along with the civil society, to manage and implement appropriate AMR control activities while being part of a collective strategy to meet the overall goal. Additionally, the National Policy on the prevention and containment of AMR and the Kenya Pharmaceutical Country Profile offer more direction in containing AMR (Government of Kenya, 2017; Ministry of Medical Services, 2010). The NAP is structured around strategic objectives in the following five areas (Table 1).

Table 1: Five strategic issues and objectives for countermeasures on AMR

| Strategic Issue | Strategic Objective |
|--------------------------------------|--|
| 1. Public Awareness and Evaluation | Improve public awareness and understanding, and promote education and training of professionals |
| 2. Surveillance and Monitoring | Continuously monitor antimicrobial resistance and use of antimicrobials, and appropriately understand the trends and spread of antimicrobial resistance |
| 3. Infection Prevention and Control | Prevent the spread of antimicrobial-resistant organisms by implementing appropriate infection prevention and control measures |
| 4. Appropriate Use of Antimicrobials | Promote appropriate use of antimicrobials in the fields of healthcare, livestock production, agriculture and aquaculture |
| 5. Research and Development | Promote research on antimicrobial resistance and foster research and development to secure the means to prevent, diagnose and treat the antimicrobial-resistant infections |

Strategic Objective 4 in the NAP focuses on optimising the use of antimicrobials in human and animal health. Prudent AMU is vital to sustainable prevention and treatment of infections.

Areas of focus in this strategic objective include:

- Developing and implementing guidelines.
- Enhancing regulations.
- Enhancing human resource capacity.
- Ensuring access to essential antimicrobials.
- Strengthening lab diagnostic capacity.

Ensuring sustainable access to quality essential antimicrobials is integral to successfully reducing the development of AMR. Consuming substandard or counterfeit antimicrobials containing less than the specified amount of the active ingredient and consuming suboptimal dosage due to lack of supply or limited access to antimicrobials contributes to the emergence of AMR. Strengthening regulatory measures, tools, and activities of the national drug regulatory agency to ensure the safety, efficacy, and quality of medicines from market

authorisation to post-marketing surveillance is key to combating AMR. Efforts must also focus on sustaining an efficient supply chain system that is geared toward ensuring the availability or accessibility of quality medicines to all patients at all times. Emphasis should be placed on appropriate use by both patients and prescribers.

Consumption of antimicrobials is influenced heavily by the cost to the consumer, and the most influential driver of consumer cost is health insurance or national health care coverage. However, in low- and middle-income countries (LMICs), the drivers are out-of-pocket expenses and exorbitant costs associated with health care access, which are enough to drive families into debt and poverty. Additionally, health care provider behaviour plays a significant role in AMU. Providers are influenced in several ways:

- By financial incentives where physicians or their institutions profit directly from antimicrobial sales.
- Patient pressure or demand for antimicrobials.
- Time of day—"decision fatigue" may set in the later hours of the day.

In hospitals in both LMICs and high-income countries, health care providers tend to prescribe empirically and are unlikely to change or discontinue an antimicrobial treatment once initiated.

1.6. Purpose of the national antimicrobial stewardship guidelines

The purpose of this guideline is to give direction to health care workers on how to establish and run AMS programmes in health care settings and the community at large. It describes the framework, approach, and available resources that support successful development and implementation of AMS in Kenya. These guidelines address the full spectrum of AMS, including development and implementation of systems, infrastructure, and interventions. Target audiences, the scope for implementation, and roles and responsibilities at various stakeholder levels are specified. Additionally, checklists and available

resources that could be leveraged to facilitate progression through the spectrum of AMS are included.

In this guidance document, stakeholders are defined in the context of national and county leadership, including the private sector, health care institutions (public and faith based), and community leadership levels. The target groups differ across levels, each with defined sets of actions. The scope of this AMS guidance document accommodates application at multiple health service centres that serve as health care points of entry, including hospitals, outpatient clinics, health centres, dispensaries, and community pharmacies. It also includes defined roles for the Pharmacy and Poisons Board (PPB). The focus of this guidance document is on human health, with linkages to the veterinary and agricultural sectors mentioned briefly.

CHAPTER 2 ANTIMICROBIAL STEWARDSHIP

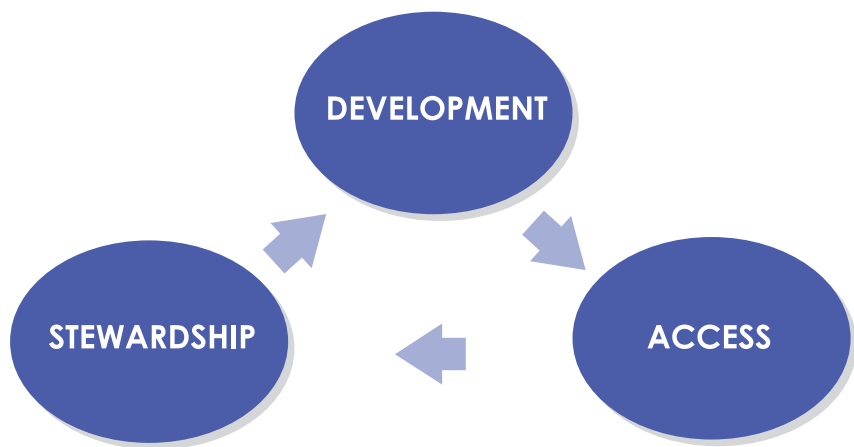
1.1. Antimicrobial stewardship

AMS refers to coordinated efforts and activities that seek to measure and improve the use of antimicrobials. In clinical practice, it entails provision of “the right antimicrobial, for the right indication (right diagnosis), the right patient, at the right time, with the right dose and route, causing the least harm to the individual patient and to future patients”.

1.2. Framework for antimicrobial stewardship

The AMS framework is built on a delicate balance between three pillars: development, access, and stewardship. Development involves advancing new antimicrobials. Access entails establishing doorways for millions of people to obtain antimicrobials when they need them. Stewardship hinges on efforts to maintain the effectiveness of existing medicines. The three pillars cannot be dealt with in isolation. Consequently, access to antimicrobials without consideration for conservation and innovation is likely to speed up resistance. AMS, on the other hand, can constrain access and undermine innovation. Furthermore, innovation without access is unjust, and access without conservation wasteful. AMS programmes should strike a balance between the three pillars, especially regions of the world with limited resources, ensuring that access to antimicrobials is not compromised and is expanded where needed.

Figure 1: Antimicrobial stewardship framework



1.3. Goals of antimicrobial stewardship

The primary goals of AMS are:

- Improving patient outcomes by reducing infection rates (including surgical site infections) and reducing morbidity and mortality.
- Improving patient safety and minimising unintended consequences of antimicrobial use, such as readmissions and adverse drug reactions.
- Reducing antimicrobial resistance through prudent use of antimicrobials.

- Reducing health care costs without adversely impacting the quality of care.

1.4. Impact of appropriate antimicrobial use on clinical and economic outcomes

There is mounting evidence that implementation of AMS programmes is a promising strategy to address appropriate use of antimicrobials and AMR. AMS programmes have been shown to reduce morbidity, mortality, and health care costs associated with infections (Table 2). These cost saving studies have been used to validate further investment into stewardship infrastructure and expansion. More recent studies have been published that have mirrored this cost saving impact.

Table 2: Antimicrobial stewardship and cost savings

| Study | Intervention | Impact |
|---------------------------------|----------------------------------|--|
| Seligman SJ et al. 1981 | Restriction | Total reduction in antibiotic costs by 29% |
| Britton HL et al. 1981 | Clinical guidelines | Total purchases of cephalosporins decreased by \$55,715 or 46.2% |
| Briceland LL et al. 1988 | De-escalation | Total cost savings of \$38,920.95 during intervention period |
| Avorn J et al. 1988 | Clinical pathway | Savings of \$76,000 annually |
| McGregor JC et al. 2014 | Computerised monitoring software | Savings of \$84,188 compared to control arm over three months |

Source: Karanika et al, 2016

Identifying national, county, and health facility data on the clinical and economic outcomes of the successful implementation of AMS programmes can serve as a standardised metric for measuring success after implementation of AMS programmes and interventions. Additionally, these data can serve other purposes, such as policy making and programme planning.

1.5. Success stories of implementing AMS programmes in LMICs

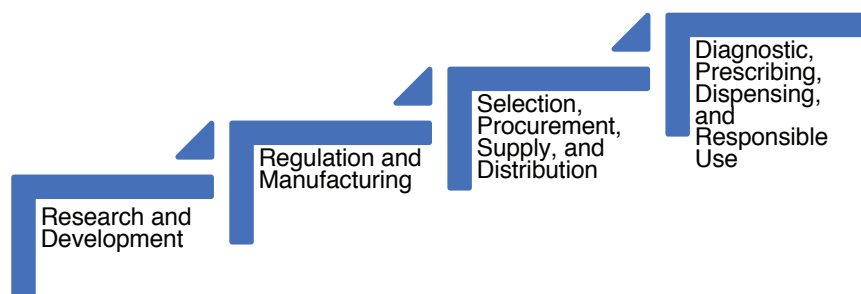
AMS programmes have been successfully implemented in South Africa, South Korea, and Taiwan. In South Africa, the stewardship programme resulted in a 12.1% reduction in defined daily doses per 100 patient-days by the first trimester of 2014. Changes in antimicrobial prescribing policies in South Korea and Taiwan led to reductions in irrational antibiotic prescribing. Similarly, in Chile, enforcement of a ban on OTC purchasing of antimicrobials resulted in a 30% reduction in antimicrobial use.

In Kenya, private hospitals like the Aga Khan University Hospital and The Nairobi Hospital have developed and implemented AMS programmes. They have observed significant adherence to antimicrobial use guidelines in surgical prophylaxis and restricted carbapenem and other reserve antibiotic use, with a resultant decline in MDR infections and candidemia. Other hospitals are in the process of developing AMS teams. It is critical that a sustainable AMS programme evaluates, incorporates, and strengthens the components in the framework for implementing AMS, research and development, and regulation and manufacturing while targeting all the steps in the medication use cycle (supply chain management, procurement, diagnosis, prescription, dispensing, use, and monitoring).

CHAPTER 3 COMPONENTS OF ANTIMICROBIAL STEWARDSHIP PROGRAMMES

In an integrated approach to optimising antimicrobial use in the context of UHC, WHO has stated the following components to be integral in AMS: regulation, supply chain management, access to antimicrobials and use, AMR surveillance, immunisation, and infection prevention and control (IPC). In the Kenyan context, we consider research and development and manufacturing as key components that have been overlooked elsewhere, and we incorporate them in our stewardship guidelines, in addition to the WHO components (Figure 2).

Figure 2: Components of the AMS implementation framework



3.1. Component 1: Research and development

The concept of research and development involves the development of new antimicrobials, diagnostic tools, vaccines, and other interventions for detecting, preventing, and controlling AMR. Research and development fundamentally support the AMS access pillar by promoting the availability of antimicrobials. A list of priority pathogens for research and development was published by WHO that focuses on 12 bacteria that pose significant threats to human health.

A monitoring and evaluation (M&E) framework is critical for measuring the impact of the component and can be used as a gauge to ensure that each component is instituted and strengthened along the pathway of implementation. Key components of M&E should be a work plan for each component that includes objectives, activities/critical action steps, expected outcome, data evaluation and measurement, the timeframe for completion, and the person/area responsible. Table 3 illustrates the gaps in research, development, manufacturing, and regulation and the proposed strategies to mitigate them, as well as the leadership and available resources.

Table 3: Gaps in research and development

| Gaps | Proposed strategies | Leadership responsibilities | Resource available |
|--|---|--|---|
| Antimicrobial resistance transmission dynamics within and among human, animal, and agriculture sectors | One Health approach through Inter-ministerial collaboration by data collation | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • One Health • FAO • Ministry of Health Quality Standards and Patient Safety Department |
| Infection prevention and control strategies, including vaccines and safe practices in all settings | Strengthening existing infection prevention and control structures in all settings | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • National Infection Prevention and Control Strategic Plan |
| Affordable, rapid, and easy-to-use | <ul style="list-style-type: none"> • Strengthening laboratory capacity through | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • MOH • Industry |

| Gaps | Proposed strategies | Leadership responsibilities | Resource available |
|---|--|--|--|
| point-of-care diagnostics | <p>LIMS and promotion for accreditation</p> <ul style="list-style-type: none"> • Conducting diagnostic stewardship for health care workers and patients • Promoting development of newer, faster, and simpler technologies | | <ul style="list-style-type: none"> • Private sector • NACOSTI • KEMRI |
| More basic and preclinical research including on microbiology and molecular mechanisms to inform the development of new anti-infective treatments | Strengthen local manufacturing processes and institutions of higher learning | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • MOH • Industry • Private sector • NACOSTI • KEMRI • Training institutions |
| Appropriate regulatory pathways that support the development of new tools to tackle AMR, including prevention, | | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • Ministry of Health • Department of Policy and Planning • World Bank • WHO |

| Gaps | Proposed strategies | Leadership responsibilities | Resource available |
|--|---------------------|--|--|
| diagnostic, and treatment tools | | | |
| New approaches from behavioural economics and other social sciences to realign incentives and make antimicrobial stewardship programmes easily adoptable and sustainable | | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • MOH • Private sector • NACOSTI • KEMRI • Training institutions |
| Burden of disease estimates and economic research on costs of action and inaction to inform local, regional, and global decision making | | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • Ministry of Health • Department of Policy and Planning • World Bank • WHO |
| Impact of veterinary and husbandry practices on the emergence and spread of | | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • One Health • FAO • Ministry of Health Quality Standards and |

| Gaps | Proposed strategies | Leadership responsibilities | Resource available |
|---|---|---|--|
| antimicrobial resistance | | | Patient Safety Department |
| Weak regulation on practices related to drug administration in the private sector | <ul style="list-style-type: none"> • Enhance inspection of pharmacies and antimicrobial selling outlets • Develop harmonised tools for assessing compliance to regulatory standards • Engage in PPB to enhance enforcement and reduce malpractice • Promote public education and public awareness of the risks associated with purchasing medicine in an unregulated environment • Carry out monitoring activities for compliance to stewardship standards | <ul style="list-style-type: none"> • National • Sub-national • Hospitals | <ul style="list-style-type: none"> • Regional and international accreditation organisations • Rebate programmes (e.g., National Health Insurance Fund) • National regulatory bodies (e.g., PPB, NQCL) |

| Gaps | Proposed strategies | Leadership responsibilities | Resource available |
|--|--|--|--|
| | <ul style="list-style-type: none"> • Standardise guidelines to support stewardship, include quality assurance models • Champion hospital accreditation programmes • Accredite and certify hospitals to enforce compliance to standards • License and relicense health facilities | | |
| Lack of quality assurance and monitoring programmes for rational use | Leveraging IT through LIMS and DHIS2 in data collection and surveillance | <ul style="list-style-type: none"> • Regional • National • County | <ul style="list-style-type: none"> • MOH • National Public Health and Quality Lab • Donor programmes (HIV, TB) |
| Lack of regulations to control waste management of pharmaceuticals | <ul style="list-style-type: none"> • Develop and strengthen policies to regulate waste disposal • Establish safe disposal programmes at sub-national levels to support | <ul style="list-style-type: none"> • National | <ul style="list-style-type: none"> • Community health structures • Pharmaceutical waste disposal structures (e.g., hospital waste disposal committees) |

| Gaps | Proposed strategies | Leadership responsibilities | Resource available |
|------|--|-----------------------------|--------------------|
| | hospitals and community health units <ul style="list-style-type: none"> • Advocate for safe disposal of antimicrobial agents in the community | | |

Source: Overcoming gaps in R&D on AMR meeting, Brasilia, 26–27th March 2015. High-level Technical Meeting. WHO, OIE, civil society organisations, Government of Brazil and other governments.

3.2. Component 2: Regulation and manufacturing

Regulation by the PPB entails efforts to enforce policies that ensure that the manufacture, import, and trade of drugs is done according to best practice and internationally accepted guidelines. The PPB also regulates the quality of medicines and any clinical trials conducted in the country.

Pharmaceutical manufacturing processes can contribute to AMR through two key routes: releasing antimicrobials into the environment in pharmaceutical waste and manufacturing antimicrobials with insufficient levels of the active antimicrobial ingredient. Regulation and manufacturing fundamentally support the AMS access pillar because they serve as the gatekeepers for the influx of new antimicrobials. Manufacturing needs to be monitored to prevent environmental emission of antimicrobials and ensure production of high-quality antimicrobials. This should be done without impeding the manufacturing process through stringent regulation.

3.3. Component 3: Supply chain: Selection, procurement, supply and distribution

Supply chain is a network of individuals, organisations, activities, resources, and technologies involved in the delivery of a product from the source to the intended institutions. Supply chain inadequacies result in antimicrobial shortages. These may lead to inadequate disease control, inappropriate antibiotic use, and the circulation and use of counterfeit or substandard antimicrobials. These inefficiencies can be caused by factors such as failures in manufacturing processes, scarcity of active pharmaceutical ingredients, pressure on margins, heavy dependence on only one or a few producers of some antimicrobials, and poor forecasting and product selection. Efficiency can be improved through demand planning, ensuring a sufficient and uninterrupted supply, and strengthening the distribution chain.

Medicines selection is a critical factor in the successful implementation of access to antimicrobials and should include assessment of the evidence base for the medicine choice and pharmaco-economic evaluations. Decisions around the selection of medicines for inclusion on a formulary or essential medicines list should also consider issues such as access and implementation.

Uninterrupted access to essential medicines of assured quality should be guaranteed. Essential medicines lists based on standard treatment guidelines should be developed through an effective evidence-based mechanism. Generally, clinical decisions regarding the selection of medicines for formularies will be made within the medical scheme comprising teams of evaluators that include medical practitioners, pharmacists, nurses, and other experts in public health and health economics. Selection of high-cost medicines should be subject to more thorough evaluation, which includes clinical efficacy and effectiveness, cost effectiveness, and budget impact.

Efficient systems for managing drug procurement and distribution should be put in place to avoid wastage or interruptions in supply.

Issues with drug quality need to be tackled through comprehensive drug regulations. Regulatory tools should be developed, and personnel appropriately trained to ensure consistency and transparency in regulatory functions. Ensuring uninterrupted supply relies on four main areas: procurement, local manufacturing, shortage mitigation, and stock management.

The pharmaceutical distribution chain can be long and intricate, involving multiple territories, factories, and warehouses. In LMICs, the chain is particularly complex, encompassing the private, public, and nongovernmental organisation market sectors. This fragmentation can lead to higher costs, longer lead times, and issues with quality. While managing these complexities is the core responsibility of governments, other stakeholders also have an influential role to play, with a focus on strengthening the distribution chain. The primary objective is to ensure that the right medicine is given to the right patient at the right time and at the right price. The four main areas of practice in this regard are:

- Information sharing through partnerships.
- Ensuring affordability.
- Ensuring quality.
- Product/packaging adaption.

Table 4 displays gaps in proposed strategies for selection, procurement, supply, and distribution; roles and responsibilities (regional leadership, national leadership, sub-national leadership, health care institution, and community leadership); and available resource to be leveraged.

Table 4: Gaps in supply and distribution

| Gaps | Strategies and solutions | Leadership responsibilities | Resources available |
|--|--|---|--|
| Quantification process not exhaustive | <ul style="list-style-type: none"> • Involve required, committed, and motivated expertise • Adopt WHO-recommended technology (information and communication technology [ICT] for categorization software) • Enforce categorising antimicrobials according to WHO list of Access, Watch, and Reserve | <ul style="list-style-type: none"> • International • National • Sub-national | <ul style="list-style-type: none"> • Lessons and structures from TB, HIV, and malaria programmes • WHO |
| Availability and relevance of Kenya National Pharmaceutical Policy and formularies | <ul style="list-style-type: none"> • Monitor policy effectiveness and update regularly | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • MOH • MTC • KEML • Publications |
| Inadequate essential medicines list | <ul style="list-style-type: none"> • Update the essential medicines list based on efficacy, quality, and cost | <ul style="list-style-type: none"> • Regional • National • Sub-national | <ul style="list-style-type: none"> • KEML |
| Lack of feedback to procurement department and MTCs | <ul style="list-style-type: none"> • Strengthening supply chain management systems • Stakeholder involvement in medicine selection | <ul style="list-style-type: none"> • Regional • National • Sub-national | <ul style="list-style-type: none"> • MTCs available in countries to guide essential |

| Gaps | Strategies and solutions | Leadership responsibilities | Resources available |
|--|---|--|---|
| | | | medicines list |
| Inadequate technical capacity for procurement officers and other staff involved in procurement | <ul style="list-style-type: none"> Education and training on medicines selection | <ul style="list-style-type: none"> Regional National Sub-national | <ul style="list-style-type: none"> IFMIS MOH MTC KEML |
| Treatment guidelines not updated regularly | Strengthening guideline review and implementation processes | <ul style="list-style-type: none"> Regional National Sub-national | <ul style="list-style-type: none"> STG reviews |
| Inadequate capacity for stock | Expansion of storage facilities in all settings | <ul style="list-style-type: none"> Regional National Sub-national | <ul style="list-style-type: none"> Central medical stores |

3.4. Component 4: Diagnostics, prescribing, dispensing and responsible use

One of the critical elements of improving AMS and drug development is the rapid and accurate identification of the pathogens and antimicrobial susceptibility testing. Effective AMS is closely linked to the ability to make the correct diagnosis. An incorrect diagnosis can lead not only to overuse or misuse of antimicrobials, particularly the critical broad-spectrum antimicrobials, but also to poor outcomes for patients resulting from failure to treat the actual disease. Lack of laboratory reagents and consumables makes proper testing, diagnosis, and treatment difficult or impossible, even when

appropriate laboratory equipment is available. Prescribers then face the hard decision of treating patients using antimicrobial agents to the best of their knowledge rather than based on an accurate diagnosis from test results.

3.4.1. Critical factors for diagnosis and treatment

The speed of diagnostic testing is a critical factor in effective AMS. The typical turnaround time using traditional microbiological testing methods is 48 to 96 hours for pathogen identification, followed by an additional 48 to 72 hours for antimicrobial drug-susceptibility testing. Initial treatment decisions may be made empirically before diagnostic testing results are available. Critical goals of AMS can be achieved through faster and more accurate diagnostic testing that reduces the time to appropriate antimicrobials; reduces unnecessary use of antimicrobials; and informs decisions regarding antimicrobial escalation, de-escalation, or discontinuation. Addressing this gap in the supply chain of diagnostic tests can make the difference between the appropriate use of antimicrobials and overuse or inappropriate use. Additionally, more significant investment in rapid diagnostics and integration into clinical practice is a key strategy.

Integration of diagnostics with other stewardship interventions to provide fast, accurate identification and susceptibility testing will achieve better clinical outcomes and timely streamlining and de-escalating of empiric broad-spectrum antimicrobials in severely ill patients. Insufficient training and supervision of health personnel, lack of access to rapid diagnostic facilities to support treatment decisions, perverse economic incentives such as profits from both prescribing and dispensing, and inappropriate marketing of pharmaceuticals can all lead to improper prescribing. The absence of legislation regulating the quality and use of antimicrobials and poor enforcement efforts fosters the unauthorised dispensing of antimicrobials by poorly trained persons and contributes to indiscriminate use.

3.4.2. National standard treatment guidelines

These should incorporate proper training and supervision of health care personnel and mechanisms to make diagnostic support available. Hospitals should have prescribing guidelines for treatment and prophylaxis for common infections relevant to the patient population, the local antimicrobial resistance profile, and the surgical procedures performed in the institution. Table 5 displays gaps in diagnostics; prescribing medicine; dispensing and responsible use; proposed strategies; roles and responsibilities (regional leadership, national leadership, sub-national leadership, health care institution, and community leadership); and available resources to be leveraged.

Table 5: Gaps in diagnosis and treatment

| Gaps | Strategies and Solutions | Leadership Responsibilities | Resources Available |
|--|--|--|--|
| <ul style="list-style-type: none"> • Inadequate laboratory capacity, resources, staffing, infrastructure, and data management • Lack of diagnostic guidelines and stewardship and noncompliance to algorithms at facilities • Inadequate prioritisation of diagnostics • Lack of confidence in laboratory services • Turnaround time for receipt of lab results • Inadequate sharing and utilisation of AMR data • Lack of national antimicrobial policy; dissemination | <ul style="list-style-type: none"> • Strengthen laboratory capacity (including LIMS) • Develop, customise, and disseminate guidelines and algorithms • Conduct diagnostic stewardship for health care workers • Sensitise patients on the importance of diagnosis before treatment • Task shift to enable nurses and phlebotomists to collect specimens • Improve laboratory clinician communication • Promote use of newer, simpler, | <ul style="list-style-type: none"> • National • Sub-national • County | <ul style="list-style-type: none"> • Ongoing efforts to strengthen laboratory capacity and surveillance (GHSA, ACDC, Fleming Fund, ASM, ASLM, AFENET, US CDC, World Bank/ECISA) • Lessons from PBF programmes in Rwanda and Burundi • MOH • NASIC • AMR secretariat |

| Gaps | Strategies and Solutions | Leadership Responsibilities | Resources Available |
|--|---|-----------------------------|---------------------|
| <p>and enforcement of treatment guidelines and algorithms</p> <ul style="list-style-type: none"> • Lack of access to essential and vital medicines and antimicrobials • Inadequate policies for distribution of antimicrobials at different levels of care • Inadequate knowledge and skills among prescribers and unqualified prescribers • Commercially driven prescribers and patient pressure on prescribers • Lack of community prescribing algorithms to mitigate access issues and stewardship | <p>and faster technologies</p> <ul style="list-style-type: none"> • Promote sharing and use of AMR data • Promote laboratory accreditation, including microbiology • Promote performance-based financing (PBF) for services • Develop national policy and disseminate and strengthen guidelines, decision making structure, and algorithms using surveillance data • Update VEN classified medicines lists • Train, sensitise, and mentor prescribers; monitor and audit prescription | | |

| Gaps | Strategies and Solutions | Leadership Responsibilities | Resources Available |
|------|--|-----------------------------|---------------------|
| | <p>habits; and provide feedback</p> <ul style="list-style-type: none"> • Restrict prescription privileges • Use of prescription software and technology • Rationalise distribution of medicines based on facility level • Define who gets the prescribing algorithms | | |

CHAPTER 4 CORE ELEMENTS FOR ANTIMICROBIAL STEWARDSHIP PROGRAMMES

Nine core elements provide a framework for effective AMS:

1. Leadership commitment and governance structure
2. Accountability
3. Drug expertise
4. Actions/interventions
5. Reporting
6. Monitoring and evaluation
7. Education and training
8. Communication
9. Quality improvement

4.1. Core element 1: Leadership commitment and governance structure

Critical components of a stewardship programme are leadership commitment and a culture of antimicrobial use. According to the Centers for Disease Control and Prevention (CDC), leadership commitment comprises dedicating necessary human resources (designating a multidisciplinary team), financial resources, and ICT resources.

4.1.1. Leadership commitment

Evidence of leadership commitment may take the form of a formal statement or policy indicating that the organisation (region, national, sub-national, or health care facility) supports efforts to improve and monitor antimicrobial use. Formal statements carry more weight with staff than informal communications such as newsletters and e-mail. It is recommended that the formal statement include stewardship-related positions or collateral duties. Subsequently, stewardship-related positions should include job descriptions and annual performance reviews. This ensures that individuals with the assigned duties are given sufficient time to contribute to stewardship activities.

Leadership commitment should reflect allocated time and resources to support training and education. As a part of the commitment, leadership should define where the organisation needs to go with regard to stewardship using quantitative data on antimicrobial use to establish organisational outcomes. Members of the organisation can then implement the vision and direction.

Table 6 describes actions of the leadership commitment, the corresponding level of leadership responsible for implementing the action, and the expertise needed.

Table 6: Leadership in antimicrobial stewardship

| Action | Role / Responsibility | Expertise | Alternate expertise |
|---|---|---|--|
| Formal or written statement to support activities to improve and monitor antimicrobial use | <ul style="list-style-type: none"> • National • Sub-national • Healthcare facilities | <ul style="list-style-type: none"> • NASIC • Consultant • Medical doctor • Pharmacist | <ul style="list-style-type: none"> • AMR secretariat • Champion physician • County pharmacist |
| Stewardship annual review | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • AMS TWG | |
| Call to action for stewardship support | <ul style="list-style-type: none"> • Regional | <ul style="list-style-type: none"> • NASIC | |
| Mobilise resources and budget for financial support to include salary support, adequate staffing, training, education, and IT support | <ul style="list-style-type: none"> • National • Sub-national • Healthcare facilities | <ul style="list-style-type: none"> • NASIC • CEO • Clinical director • Medical superintendent | |

| Action | Role / Responsibility | Expertise | Alternate expertise |
|---|---|---|---|
| Allocated time to participate in stewardship activities, including training and education | <ul style="list-style-type: none"> • National • Sub-national • Healthcare facilities | <ul style="list-style-type: none"> • NASIC • CEO • Clinical director • Medical superintendent | <ul style="list-style-type: none"> • MTC |
| Establish stewardship-related duties in job descriptions and annual performance reviews | <ul style="list-style-type: none"> • National • Sub-national • Healthcare facilities | <ul style="list-style-type: none"> • CEO • Clinical director • Medical superintendent | <ul style="list-style-type: none"> • Supervisors |
| Designate a multidisciplinary stewardship team | <ul style="list-style-type: none"> • National • Sub-national • Healthcare facilities | <ul style="list-style-type: none"> • CEO • Clinical director • Medical superintendent | <ul style="list-style-type: none"> • MTC |
| Leadership should establish clear communication on antimicrobial stewardship strategies | <ul style="list-style-type: none"> • National • Sub-national • Healthcare facilities | <ul style="list-style-type: none"> • AMS Committee leaders | <ul style="list-style-type: none"> • MTC |

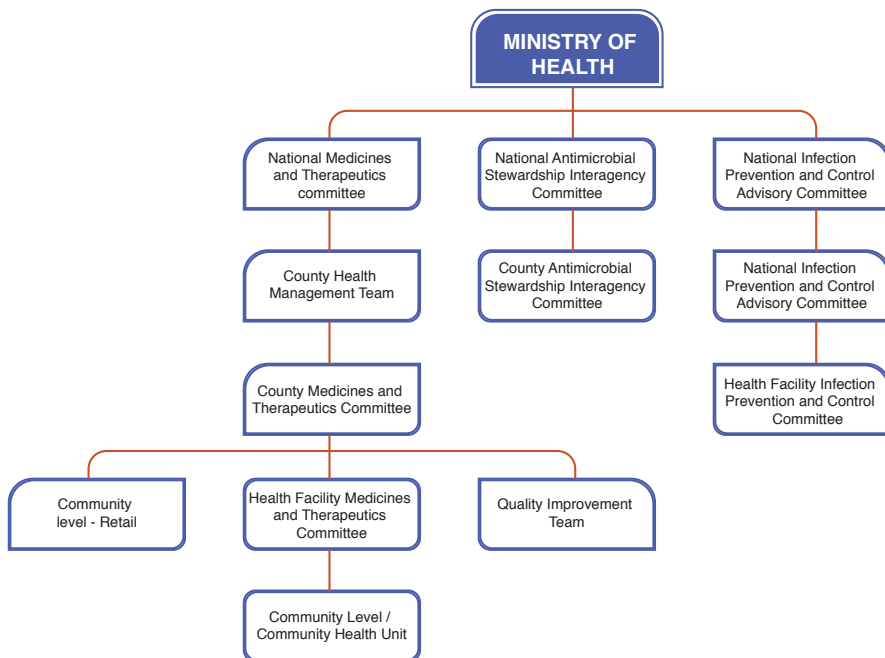
4.1.2. Governance structures

Following an organisation's declared commitment to AMS, leadership needs to establish the governance structure for the stewardship programme. The governance structure is important in sustaining the programme since it provides the required decision-making chain, authority, and oversight structures. It encompasses the combination of individuals filling executive and management roles, programme oversight functions, and structure and policies that define management principles and decision making.

The governance structure at the national level is responsible for setting the AMR strategy and mission and directing country-specific outcomes. The national level is also responsible for ensuring a collaborative, integrated approach to animal and human AMS interventions. There may already be national programmes, such as the National MTC, HIV, TB, and malaria, with governance structures that could accommodate AMS activities. However, it is essential to define lines of communication, reporting, and accountability clearly. Subcommittees could also be designated to investigate and report on the AMS strategy.

At the sub-national level, organisations within the counties, sub-counties, and health establishments play a vital role in operational oversight of the AMS programme in support of national governance. The governance structure at the sub-national level is responsible for taking the national strategic objectives and standards and adapting them to suit operational model and governance structures. It ensures that budgets are set up to support stewardship activities, provide M&E functions to determine progress, conduct situational analyses, and prioritise and implement AMS interventions.

Figure 3: Governance structures for antimicrobial stewardship



AMS governance typically falls within the clinical leadership functions of the heads of county and sub-county departments of health. Depending on resources and capacity, governance functions could also include pharmaceutical and therapeutic monitoring and IPC monitoring. To leverage resources, organisations should consider using governance structures already in place that can accommodate AMS activities.

Successful programmes at the health care facility level have typically placed AMS governance within the hospital’s quality improvement and

patient safety governance structure and included them in the hospital's quality and safety strategic plan. The responsibility for implementing and managing the AMS programme resides with a multidisciplinary AMS team or committee.

It is important to have formal links established among the AMS committee, hospital executive (alternative hospital head of clinical services), director of clinical services (alternative physician/clinical pharmacist), MTC (alternative clinical pharmacist/quality of care committee), and Infection Prevention and Control Committee (IPCC) (alternative Quality of Care Committee). It is critical that the highest-ranking member of each component represents the hospital on the AMS committee to ensure translation of policy into action. Figure 4 provides an example of a governance structure with a reporting framework for an AMS committee that could be adapted to different hospital structure.

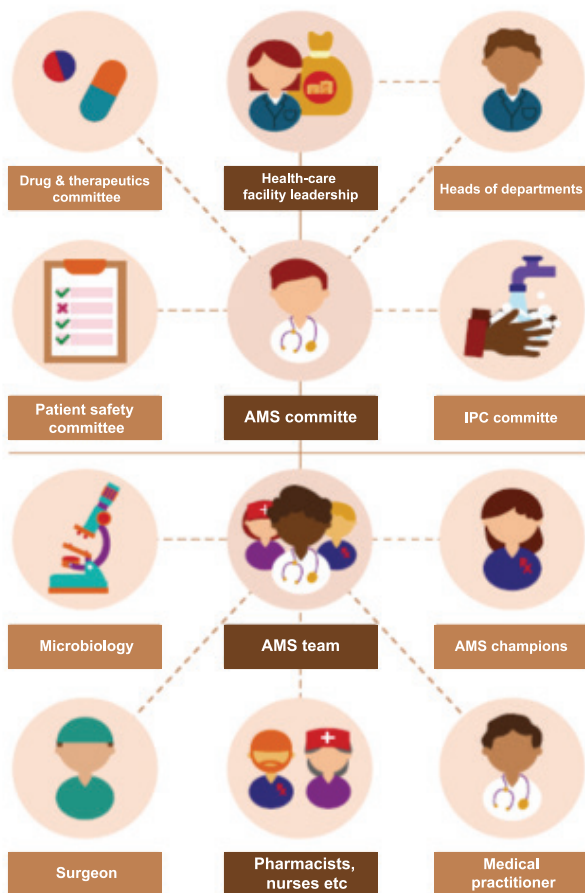
The recommended membership of the AMS committee includes a clinician, clinical microbiologist, infectious disease expert, clinical pharmacist, specialist nurses, patient safety manager, and an ICT expert. As a minimum, the AMS committee should include an appropriate physician (a clinical microbiologist or infectious disease [ID] physician, if available) and a clinical pharmacist (with ID training if possible) or pharmacist as core team members. Where on-site ID physicians or clinical microbiologists are not available, the AMS Committee should be led by a clinician who champions the responsible use of antimicrobials. Where resources are scarce and the above-described expertise is not available, facilities may negotiate appropriate external specialist advice to support the local AMS Committee. Small hospitals without an on-site pharmacist should consider working with a clinical pharmacist (e.g., from a regional hospital).

As the prescribers of antimicrobials, it is vital that clinicians are fully engaged in and support efforts to improve antimicrobial use in

hospitals. Laboratory staff can guide the proper use of tests and the flow of results. They can also guide empiric therapy by creating and interpreting a health facility antibiogram. ICT staff are critical to integrating stewardship protocols into existing workflow. An example is embedding information and protocols at the point of care, such as immediate access to facility-specific guidelines at the point of prescribing, implementing clinical decision support for antimicrobial use, creating prompts for action to review antimicrobials in key situations, and facilitating the collection and reporting of AMU data.

Nurses can ensure that samples for culture and sensitivity testing are taken before initiating antimicrobials. Nurses review medications as part of their routine duties and can prompt discussions of antimicrobial treatment, indication, and duration. Infection preventionists and hospital epidemiologists can assist with auditing, analysing, monitoring, and reporting of resistance trends; educate staff on the importance of appropriate AMU; and implement strategies to optimise the use of antimicrobials. There is no consensus on staffing recommendations; however, hospitals with existing programmes suggest that for every 100 patient beds, at least 10 hours of clinical pharmacist and 3.5 hours of lead clinician time per week should be dedicated to AMS activities. WHO's AMS guidelines can be used to guide institutions on staffing and other stewardship requirements.

Figure 4: AMS governance structure



Source: Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries. A practical toolkit. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO.

4.2. Core element 2: Accountability

Successful programmes have shown that accountability and drug expertise are critical for a successful stewardship programme. The recommendation is to appoint a single leader who will be responsible for the stewardship programme outcomes, preferably a physician. Formal training in infectious diseases and AMS would benefit

stewardship programme leaders. Locations with available resources and capacity have achieved success by hiring full-time staff to develop and manage stewardship programmes; however, with limited resources, options include the use of part-time and off-site expertise from other hospitals. An MTC can expand its role to assess and improve antimicrobial use.

The stewardship leader and co-leader should be incorporated into the AMS governance structure and linked to the AMS Committee. Clear lines of accountability among the AMS governance structure and other existing governance structures, such as the clinical governance, MTC, and IPCC, should be established.

Responsibilities associated with stewardship programme accountability and drug expertise differ at different levels of leadership. Table 7 describes actions of the accountability and drug expertise element and the corresponding level of leadership responsible for implementing the action and expertise needed.

4.3. Core element 3: Drug expertise

In the hospital setting, the role of the pharmacist has become a significant component of ensuring the success of AMS programmes. To co-lead the programme, a pharmacist responsible for improving AMU is needed. The expertise of the clinical pharmacist can directly impact and improve patient safety by helping guide appropriate antimicrobial therapy. Because of their roles in the hospital, pharmacists are able to see the entire medications picture in the institution as well as the individual scenarios at the patient and unit levels, and this helps in stewardship efforts. Pharmacists are perfectly situated to see global antibiotic use in the hospital as well as guide specific medication regimens to ensure that they are optimal.

Table 7: Core elements 2 and 3: Accountability and drug expertise

| Action | Role / Responsibility | Expertise | Alternate Expertise |
|---|---|---|--|
| Designate a leader and co-leaders to be accountable to leadership for meeting established goals and targets | <ul style="list-style-type: none"> • Healthcare facilities | <ul style="list-style-type: none"> • Infectious disease physician • Pharmacist | <ul style="list-style-type: none"> • In the absence of both, identify an appropriate champion for the programme |
| Ensure that the leadership of the AMS programme has received training in antimicrobial stewardship | <ul style="list-style-type: none"> • National • Sub-national • Healthcare facilities | <ul style="list-style-type: none"> • NASIC • AMR secretariat • AMS committee | <ul style="list-style-type: none"> • AMS champion |
| Appoint a pharmacy to co-lead efforts to improve the use of antibiotics within the facility | <ul style="list-style-type: none"> • Healthcare facilities | <ul style="list-style-type: none"> • Clinical pharmacist | <ul style="list-style-type: none"> • Pharmacist • Pharmaceutical technologist |
| Set standards for antibiotic prescribing | <ul style="list-style-type: none"> • Healthcare facilities | <ul style="list-style-type: none"> • AMS committee • ID specialist • Clinical pharmacist | |
| Set practice standards for assessing, monitoring, and communicating changes in patient conditions | <ul style="list-style-type: none"> • Healthcare facilities | <ul style="list-style-type: none"> • ID specialist • Champion physician | <ul style="list-style-type: none"> • Physician/clinician |

| Action | Role / Responsibility | Expertise | Alternate Expertise |
|--|---|---|---|
| Identify/recommend appropriate staff to champion antimicrobial stewardship | <ul style="list-style-type: none"> • Health centres and clinics | <ul style="list-style-type: none"> • Clinician in charge | <ul style="list-style-type: none"> • Nurse in charge |
| Establish an antimicrobial stewardship team to include microbiologist, IT staff, nurses, infection preventionists, health promotion, procurement, and hospital epidemiologists | <ul style="list-style-type: none"> • Sub-national • Healthcare facilities | <ul style="list-style-type: none"> • AMS chair | <ul style="list-style-type: none"> • AMS team |

4.4. Core element 4: Actions/Interventions

Policies and guidelines that support optimal antimicrobial prescribing should be developed and implemented at the national, county, and health facility levels. Furthermore, interventions need to be selected based on the needs of a country, county, or health care facility as well as the availability of resources and expertise. AMS programmes should be careful not to implement too many interventions at once.

4.5. Core element 5: Reporting

Reporting information collected on antimicrobial use and resistance patterns to doctors, pharmacists, nurses, and staff on a regular basis serves as a reminder of the importance of AMS activities. Regular reporting should occur within the organisation and to external leadership levels that have responsibility for AMS. Ideally, reporting elements should focus on consumption and resistance trends in addition to patient outcomes to assess the impact of interventions,

identify potential areas for improvement, and provide feedback to clinicians.

Reducing AMR is another important goal of AMS and should be reported on, particularly for specific patient care locations with active stewardship interventions. Reporting could focus on the evaluation of processes, such as whether prescribers documented treatment indications, adhered to facility-specific treatment guidelines, obtained appropriate diagnostic tests, or modified antimicrobial choices to microbiological findings. Responsibilities associated with stewardship programme reporting actions differ at different levels of leadership. Table 8 describes actions of reporting elements, the corresponding level of leadership responsible for implementing the action, and the expertise needed.

Table 8: Core element 5: Reporting

| Action | Role / Responsibility | Expertise | Alternate Expertise |
|---|--|--|--|
| Harmonise the reporting system to ensure flow of information | <ul style="list-style-type: none"> • Regional • National | <ul style="list-style-type: none"> • AMR secretariat | <ul style="list-style-type: none"> • Advocacy TWG |
| Disseminate antibiogram and consumption information by specific community within the nation | <ul style="list-style-type: none"> • National • Sub-national | <ul style="list-style-type: none"> • Surveillance TWG | <ul style="list-style-type: none"> • Advocacy TWG |
| Provide guidelines to standardise antibiogram development | <ul style="list-style-type: none"> • National | <ul style="list-style-type: none"> • Surveillance TWG | |

| Action | Role / Responsibility | Expertise | Alternate Expertise |
|--|---|--|---|
| Ensure agreed upon reporting up to the regional level | <ul style="list-style-type: none"> National Sub-national | <ul style="list-style-type: none"> Surveillance TWG | <ul style="list-style-type: none"> Advocacy TWG |
| Share data collected with all health care providers as well as leadership and any other stakeholders | <ul style="list-style-type: none"> National Sub-national Healthcare facilities | <ul style="list-style-type: none"> Surveillance TWG Microbiology laboratory AMS Committee | |
| Leverage existing information systems within the country to support reporting of resistance and use | <ul style="list-style-type: none"> Sub-national | | |
| Produce regular reports on antibiotics that are being tracked in the facility | | <ul style="list-style-type: none"> Pharmacist AMS Committee | <ul style="list-style-type: none"> Nurse in charge |
| Share updates and improvements with leadership, physicians, and other stakeholders | | <ul style="list-style-type: none"> AMS Committee | |

4.6. Core element 6: Monitoring and evaluation

The key for this element is monitoring and evaluating antimicrobial prescribing practices and processes and their impact on resistance patterns. Success of this element lies in measurement, as only things that are measured are managed. Mechanisms and IT systems are needed to report and analyse antimicrobial use and resistance as part

of local and regional efforts to reduce antimicrobial-resistant infections through AMS.

To evaluate whether antimicrobial prescribing is rational, data on the number of prescriptions, indications, laboratory results before transitioning to second line and higher antimicrobials, dose, and duration of treatment, as well as different sub-groups, are essential. Such data are needed to evaluate the impact of antimicrobial prescribing on resistance, morbidity, complications, and mortality.

Adherence to facility-specific treatment recommendations, documentation of antimicrobial indication, and adherence to indication documentation policy are paramount. Standardised tools, such as those for drug use evaluations or antimicrobial audit forms developed by the CDC, can assist in these reviews. Retrospective charts reviews could also be used based on pharmacy records or discharge diagnoses. It is important to document interventions, provide feedback, and track responses to feedback.

Antimicrobial use can be measured as either days of therapy (DOT) or defined daily dose (DDD). DOT is an aggregate sum of days for which any amount of a specific antimicrobial agent is administered or dispensed to a particular patient (numerator) divided by a standardised denominator (e.g., patient days, days present, or admissions). An alternative measure of antimicrobial use is DDD. This metric estimates antimicrobial use in hospitals by aggregating the total number of grams of each antimicrobial purchased, dispensed, or administered during a period of interest divided by the WHO-assigned DDD.

It is important to monitor and evaluate clinical outcomes that measure the impact of interventions to improve AMU. Improving AMU has a significant impact on rates of hospital-onset *Clostridium difficile* infections and could be a target for stewardship programmes. Reducing AMR is another important goal for efforts to improve AMU

and presents another option for measurement. The impact of stewardship interventions on resistance is best assessed when the measurement is focused on pathogens that are recovered from patients after admission (when patients are under the influence of the stewardship interventions). Monitoring resistance at the patient level (i.e., what percentage of patients develop resistant super-infections) has also been shown to be useful.

The pitfalls in implementing this core element are varying data collection systems, time periods, and units of measurements. These make it difficult to compare trends in antimicrobial usage across the regions and within the country. As such, definition and standardisation of these factors are recommended before implementing stewardship interventions. Responsibilities associated with stewardship M&E actions differ at different levels of leadership.

Table 9 describes actions of the reporting element, the corresponding level of leadership responsible for implementing the action, and the expertise needed.

Table 9: Core element 6: Monitoring and evaluation

| Action | Role / Responsibility | Expertise | Alternate Expertise |
|---|---|--|--|
| Collect data on antimicrobial use and infection rates that are indicators for antimicrobial use | <ul style="list-style-type: none"> • Healthcare facilities | <ul style="list-style-type: none"> • Pharmacist • Microbiologist • Epidemiologist • IT staff | |
| Monitor antimicrobial use, antimicrobial prescribing, and antimicrobial resistance | <ul style="list-style-type: none"> • Regional • National • Healthcare facilities | <ul style="list-style-type: none"> • Pharmacist • Microbiologist • Epidemiologist • IT staff | |
| Evaluation of country-level interventions | <ul style="list-style-type: none"> • Regional • National | <ul style="list-style-type: none"> • NASIC • AMR TWGs • IT | |
| Establish metrics for evaluating country status on antimicrobial use, antimicrobial prescribing, and antimicrobial resistance | <ul style="list-style-type: none"> • National • Healthcare facilities | <ul style="list-style-type: none"> • NASIC • AMR TWGs • IT | |
| Ensure inclusion of a quality improvement programme for routine evaluation of specific interventions | <ul style="list-style-type: none"> • National/sub-national • Healthcare facilities | <ul style="list-style-type: none"> • NASIC • AMR TWGs • IT | |
| Collect data to monitor whether prescribers have accurately applied diagnostic criteria for infection | <ul style="list-style-type: none"> • Healthcare facilities | <ul style="list-style-type: none"> • AMS Committee • Physician • Microbiologist | <ul style="list-style-type: none"> • Pharmacist • Clinician • Nurse |

| Action | Role / Responsibility | Expertise | Alternate Expertise |
|--|---|--|---|
| Collect data on documented indication and planned duration of antibiotic therapy and obtained cultures and relevant tests prior to treatment | <ul style="list-style-type: none"> Healthcare facilities | <ul style="list-style-type: none"> Pharmacist Microbiologist | <ul style="list-style-type: none"> Physician Clinician Nurse |

4.7. Core element 7: Education and training

While education alone is not sufficient, it is vital to any successful AMS programme. Continued AMS education should be provided to physicians, pharmacists, nurses, and other staff. Education and training should focus on AMR and improving antimicrobial prescribing and dispensing practices. Educational programmes can provide a foundation of knowledge that will work to enhance and increase acceptance of stewardship strategies. Education should also be provided to patients and family members when possible; consumer awareness of AMS can be raised using the CDC Get Smart tools.

There are many options for providing education on AMU, such as educational presentations in formal or informal settings, messaging through posters and flyers, and newsletters or electronic communications to staff groups. Reviewing de-identified cases with providers where changes in antimicrobial therapy could have been made is another useful approach. A variety of web-based educational resources are available that can help facilities develop educational content. Education has been found to be most effective when paired with corresponding interventions and measurement of outcomes.

Clinical messages could be targeted to clinicians, prescribers, and patients. Identify and communicate to prescribers’ specific situations where antimicrobials should be withheld, and offer guidance

concerning the duration of AMU, which is often an area of misuse. Communicating, sharing, and learning from data is also essential. Face-to-face or electronic meetings with prescribers, where there is an opportunity for reflection about their prescribing practices, is critical in promoting learning about prudent prescribing. Responsibilities associated with stewardship education and training actions differ at different levels of leadership. Table 10 describes actions of the education and training element, the corresponding level of leadership responsible for implementing the action, and the expertise needed.

Table 10: Core Element 7: Education and training

| Action | Role / Responsibility | Expertise | Alternate Expertise |
|--|---|--|---|
| Develop a curriculum-based programme on antimicrobial stewardship | <ul style="list-style-type: none"> • Regional • National | <ul style="list-style-type: none"> • NASIC • AMR TWGs | <ul style="list-style-type: none"> • AMR secretariat |
| Provide continuous professional development trainings | <ul style="list-style-type: none"> • Regional • National • Healthcare facilities | <ul style="list-style-type: none"> • ID specialist • Clinical pharmacist | <ul style="list-style-type: none"> • Clinical microbiologist |
| Establish training programme for the community health volunteers | <ul style="list-style-type: none"> • Regional • National | <ul style="list-style-type: none"> • NASIC • AMR TWGs | <ul style="list-style-type: none"> • AMR secretariat |
| Adopt and support capacity building for stewardship training programme | <ul style="list-style-type: none"> • Sub-national | <ul style="list-style-type: none"> • NASIC • AMR TWGs | <ul style="list-style-type: none"> • AMR secretariat |

| | | | |
|---|---|--|--|
| Education and training of staff using locally generated information | <ul style="list-style-type: none"> • Healthcare facilities | <ul style="list-style-type: none"> • ID specialist • Clinical pharmacist | <ul style="list-style-type: none"> • Clinical microbiologist |
| Provide education on a regular basis to staff, patients, and families | <ul style="list-style-type: none"> • Healthcare facilities | <ul style="list-style-type: none"> • AMS team | <ul style="list-style-type: none"> • Pharmacist • Nurse • Clinician |
| Incorporate antimicrobial stewardship elements into orientation for new medical staff | <ul style="list-style-type: none"> • Healthcare facilities | <ul style="list-style-type: none"> • AMS team • Management staff | <ul style="list-style-type: none"> • Pharmacist • Nurse • Clinician |
| Use evidence base through data collected to educate physicians | <ul style="list-style-type: none"> • Healthcare facilities | <ul style="list-style-type: none"> • AMS team | <ul style="list-style-type: none"> • Pharmacist • Nurse • Clinician |

4.8. Core element 8: Communication

Communication is a vital component of the success of an AMS programme. Evidence has shown that effective communication campaigns contribute to promoting the rational use of antimicrobials by prescribers and patients, as well as within the agriculture and food industries. Communication frameworks should contain clear, straightforward communication that shows the vision and the benefits of the programme, core clinical messages, and mechanisms for internal and external communication with stakeholders. The design and implementation of the framework needs to be well defined and strategic and should incorporate essential elements of effective communication campaigns.

Certain design elements are recommended in a communication campaign to ensure effectiveness and impact. These include multipronged communication plans involving a mix of media channels; audience segmenting and audience-centric messaging; targeted messaging; the timing of campaign activities; involvement of key

opinion leaders; and phase-wise evaluation (formative, process, and summative evaluations).

Responsibilities associated with stewardship communication actions differ at different levels of leadership. Table 11 describes actions of the communication element, the corresponding level of leadership responsible for implementing the action, and the expertise needed.

Table 11: Core element 8: Communication

| Action | Role / Responsibility | Expertise | Alternate Expertise |
|--|---|--|--|
| Dissemination of evidence-based best practices from different countries | <ul style="list-style-type: none"> National | <ul style="list-style-type: none"> NASIC | <ul style="list-style-type: none"> AMR TWGs |
| Support and champion capacity for knowledge management | <ul style="list-style-type: none"> National | <ul style="list-style-type: none"> NASIC | <ul style="list-style-type: none"> AMR TWGs |
| Awareness campaign and communication messaging | <ul style="list-style-type: none"> National | <ul style="list-style-type: none"> NASIC | <ul style="list-style-type: none"> Surveillance TWG |
| Develop, implement, and sustain an awareness campaign, communication messaging, and targeted messaging | <ul style="list-style-type: none"> Sub-national Healthcare facilities | <ul style="list-style-type: none"> Surveillance TWG | |
| Create and sustain a system for knowledge management | <ul style="list-style-type: none"> Sub-national Healthcare facilities | <ul style="list-style-type: none"> Surveillance TWG IT staff | |

| | | | |
|---|---|--|--|
| Establish processes and champions to support and sustain dissemination of best practices from different countries | <ul style="list-style-type: none"> • Sub-national • Healthcare facilities | <ul style="list-style-type: none"> • NASIC | <ul style="list-style-type: none"> • Surveillance TWG |
| Develop a system with capability for alerts and notification within the antimicrobial stewardship process | <ul style="list-style-type: none"> • Sub-national • Healthcare facilities | <ul style="list-style-type: none"> • Surveillance TWG | |

4.9. Core element 9: Quality improvement

Quality improvement can be incorporated into a stewardship programme to ensure that interventions are continuously improved, and efforts are sustained. Changes and interventions should be tested using experiential learning methods, such as the Plan-Do-Study-Act (PDSA) cycle, before they are permanently implemented. Testing in quality improvement allows unforeseen problems to be resolved and interventions to be evaluated and refined before full implementation into day-to-day operations. Each PDSA sequence should increase in scope and scale and be analysed, allowing subsequent tests to be refined.

Selection of an intervention or change should be based on drivers that impact the goals of AMS. Stewardship goals are influenced by primary and secondary drivers that impact the outcome of the goal. Primary drivers of timely and appropriate use of antimicrobial utilisation include timely and appropriate initiation of antimicrobials, appropriate administration and de-escalation, data monitoring and stewardship infrastructure, and availability of expertise at the point of care. When a primary or secondary driver has been selected for change, it is critical to outline the quality improvement steps:

1. Clearly establish the aim – What are we trying to accomplish?
2. Establish a measure – How will we know that a change is an improvement?

3. Plan to improve – What changes can we make that will result in improvement?
4. A specific test of changes – Perform the PDSA cycle.

The P in the PDSA cycle stands for Plan and covers the planning phase of the cycle. This phase should address questions related to ideas for change; questions and predictions; plans for who, what, where, and when for the cycle; and plans for data collection. The D means Do and covers the phase of the cycle where the action is carried out. This involves carrying out the plan and documenting problems and unexpected observations. The S means Study and involves analysis of the data, comparison of the data and findings to the predictions, and summary of lessons learned. The A means Act and involves establishing what changes need to be made for the next cycle. Quality improvement requires repeated use of the PDSA cycle to ensure that changes result in improvement.

This is an example of the application of the PDSA cycle for AMS in a hospital. Assume the AMS team decides to introduce a restricted antimicrobial formulary, with required prior phone approval from an ID physician, before selected agents are dispensed. They would be wise to initially test the approval and dispensing process in a range of conditions. For example, they could work with one cooperative prescriber to see if the process works well at different times of the day, on weekends, and when different dispensing pharmacists or ID physicians are on duty. After making any necessary refinements, the team could then plan on including all respiratory patients, then all medical patients, and so on.

Table 12: Summary of Core Elements

| | Level 1 | Level 2 | Level 3 | Level 4 | Level 5 | Level 6 |
|---------------------------|-------------------------------------|--------------------------------------|--|---|---|---|
| Leadership | AMS champion | AMS champion | AMS link nurse | AMS Committee led by a physician | AMS Committee led by an ID physician | AMS Committee led by an ID physician |
| Governance | Champion reports to nurse in charge | Nurse reports to clinician in charge | Nurse/clinician/pharmaceutical technologist Reports to county pharmacist Linked to IPC | Core team: Physician, microbiologist, technician, pharmacist, IT staff, IPC, nursing Reports to CEO/medical superintendent/MTC Linked to IPC, patient safety, clinical governance, QC | Core team: ID physician, clinical microbiologist, clinical pharmacist, IT staff, IPC, nursing Reports to CEO/DCS/MTC Linked to IPC, patient safety, clinical governance, QC | Core team: ID physician, clinical microbiologist, clinical pharmacist, IT staff, IPC, nursing Reports to CEO/DCS/MTC Linked to IPC, patient safety, clinical governance, QC |
| Accountability | Designated staff | Designated staff | Works with IPC team or MTC | Chaired by physician/pharmacist | Chaired by ID specialist/clinical microbiologist | Chaired by ID specialist/clinical microbiologist |
| Drug expertise | Designated staff | Pharmaceutical technologist | Pharmacist | Clinical pharmacist | Clinical pharmacist | Clinical pharmacist |
| Reporting | Nurse | Nurse Clinician | Pharmacist Microbiologist | Pharmacist Microbiologist | Pharmacist Microbiologist | Pharmacist Microbiologist |
| Monitoring and evaluation | Nurse | Nurse Clinician | Pharmacist Microbiologist | Pharmacist Microbiologist | Pharmacist Microbiologist Epidemiologist | Pharmacist Microbiologist Epidemiologist |
| Education and training | Designated staff | Designated staff | Designated staff | Designated staff | Designated staff | Designated staff |
| Communication | Designated staff | Designated staff | Designated staff | AMS team/physicians/pharmacists/IPC/QC/patient | AMS team/physicians/pharmacists/IPC/QC/patient | AMS team/physicians/pharmacists/IPC/QC/patient |
| Quality improvement | Designated staff | Designated staff | Designated staff | Designated staff | Designated staff | Designated staff |

CHAPTER 5 ACTIONS AND EFFECTIVE INTERVENTIONS TO SUPPORT ANTIMICROBIAL STEWARDSHIP

AMS actions and interventions are categorized as national, county, facility, community pharmacy, and community based. All actions and interventions require varying levels of capacity and resources to be implemented.

5.1. National level actions and interventions

The National Antimicrobial Stewardship Interagency Committee Technical Committee

(NASIC-TC), comprising technical directors of relevant ministries and experts, shall be responsible for overseeing the implementation of the National Policy for AMR, which includes AMS activities. The NASIC AMS TWG shall be responsible for formulating, monitoring, and evaluating implementation of AMS activities in the AMR national action plan. These activities include:

- Developing a national action plan on AMS activities.
- Developing, updating, and ensuring access to the Kenya Essential Medicines List (KEML).
- Creating and promoting evidence-based treatment guidelines for common clinical syndromes.
- Participating in AMR awareness campaigns.
- Promoting diagnostic stewardship.
- Supporting inclusion of AMS training in pre-service curricula, in-service programmes, continuing professional development programmes, and stand-alone courses.
- Supporting and enforcing policies requiring prescriptions for antimicrobials.
- Tracking antimicrobial dispensing using available data and setting national targets for improvement.
- Measuring antimicrobial consumption (AMC) and assessment of appropriateness

- Describing resistance patterns to improve treatment guidelines and identify priority pathogens.
- Monitoring antimicrobial quality.
- Addressing drivers of inappropriate prescribing behaviour.

5.2. County level actions and interventions

The County Antimicrobial Stewardship Interagency Committee (CASIC), comprising County Executive Committee members, County Chief Officers of relevant departments, Technical County Directors, and experts, shall be responsible for approving budgets and work plans, resource mobilisation, and implementation of the AMR NAP at the county level, which includes AMS activities. The CASIC AMS TWG shall be responsible for:

- Developing and implementing county action plans on AMS activities.
- Ensuring access to and implementation of the KEML at the county level.
- Promoting use of evidence-based treatment guidelines for common clinical syndromes.
- Participating in AMR awareness campaigns.
- Promoting diagnostic stewardship.
- Supporting implementation of AMS pre-service, in-service, and continuing professional development training programmes.
- Supporting and enforcing policies requiring prescriptions for antimicrobials.
- Tracking and improving antimicrobial dispensing using available data and submitting reports to the national level.
- Measuring AMC and assessing appropriateness.
- Tracking AMR patterns, identifying priority pathogens, and submitting reports to the national level.
- Monitoring antimicrobial quality.
- Addressing drivers of inappropriate prescribing behaviour.

5.3. Hospital-based interventions (Levels 6, 5 and 4)

5.3.1. Core interventions

5.3.1.1. *Clinical review and direct prescriber feedback*

The AMS team shall oversee the clinical review of patients and provide guidance and feedback to prescribers regularly. The review of antimicrobial prescribing can be prospective or retrospective. Prospective review can involve strategies such as preauthorisation and antimicrobial restrictions, with immediate feedback being provided to the prescriber before the antimicrobial is administered.

The AMS team shall have a system for timely identification of patients who are receiving or are likely to require antimicrobial therapy and who are likely to benefit from an AMS intervention.

The decision on which patients require bedside review may be based on formal requests for consultation; laboratory results (in particular, positive cultures from normally sterile sites); regular ward rounds in high-risk areas (such as intensive care units); or lists of patients receiving restricted antimicrobials, prolonged duration, or unusual combinations of antimicrobials. The AMS team should carry out a clinical review of selected patients and, where necessary, provide advice on optimal antimicrobial therapy to the clinician/team responsible for the patient's care.

This advice may be provided via:

- Direct conversation with the clinician/team (preferred).
- The clinical pharmacist attending the AMS team ward round.
- Written records in the patient's medical record (in addition to direct conversation, particularly in the setting of a formal clinical consultation by members of the AMS team).
- Written advice on a standardised form.
- Innovative electronic media, such as mobile applications.

Prescriber feedback following clinical review shall be seen as optional advice that does not interfere with the prescriber's clinical autonomy, be delivered in a non-confrontational and non-critical manner and be used as an opportunity to educate prescribers on the principles of prudent AMU.

5.3.1.2 Restricted availability of antimicrobials and preauthorisation

Health facility antimicrobial prescribing guidelines shall include a list that stipulates which antimicrobials are Access, Watch, and Reserve. Criteria for Reserve antimicrobials shall include spectrum of activity, potential toxicity, misuse, cost, and high resistance potential, among others.

The list of Reserve antimicrobials shall be reviewed on a regular basis in light of the hospital's antimicrobial usage data and rates of AMR. Restrictions may have to be reinforced or applied to additional antimicrobial agents in cases of outbreaks caused by antimicrobial-resistant pathogens (e.g., *C. difficile*, vancomycin-resistant enterococci, MRSA).

Reserve antimicrobials shall only be available from the hospital pharmacy and not included in ward drug stocks. However, hospitals should ensure that there is a mechanism for accessing Reserve agents, when required, outside of normal working hours. Where possible, each hospital should have a process in place to allow preauthorisation for the use of Reserve antimicrobials by a member of the AMS team.

Where preauthorisation is not possible, there should be a system for identifying when Reserve antimicrobials have been prescribed and for early review of such prescriptions by a member of the AMS team.

5.3.2. Complementary interventions

5.3.2.1. Guidelines and clinical pathways

Healthcare facilities should have local or regional antimicrobial prescribing guidelines for specific syndromes, based where possible on local AMR data (antibiogram). Guidelines should be evidence based and developed in collaboration with health care facility clinicians; updated regularly; and available to all prescribers, including in electronic and other user-friendly formats such as pocket-size cards. These guidelines should not interfere with prompt and effective treatment for severe infection or sepsis. The guidelines for specific syndromes may include those for antimicrobial surgical prophylaxis, acute pharyngitis, acute infectious diarrhoea, ventilator-associated pneumonia, acute otitis media, urinary tract infections (UTIs), skin and soft tissue infections, and blood stream infections, among others. AMS guidelines on the management of some infections are described below.

- **Community-acquired pneumonia**
Improving diagnostic accuracy, tailoring of therapy to culture results, and optimising duration of treatment are important.
- **Urinary tract infections**
Many patients who get antibiotics for UTIs have asymptomatic bacteriuria and not infections. Guidelines for UTIs should focus on avoiding unnecessary urine cultures and treatment of patients who are asymptomatic and ensuring that patients receive appropriate therapy based on local susceptibilities and for the recommended duration.
- **Skin and soft tissue infections**
Guidelines for skin and soft tissue infections should focus on ensuring that patients are not prescribed antibiotics with overly broad spectra and ensuring correct duration of treatment.

- **Empiric coverage of MRSA infections**
 In many cases, therapy for MRSA can be stopped if the patient does not have an MRSA infection or changed to a beta-lactam if the cause is methicillin-sensitive *Staphylococcus aureus*.
- ***Clostridium difficile* infections**
 Treatment guidelines for *Clostridium difficile* infections (CDI) should urge providers to stop unnecessary antibiotics in all patients diagnosed with CDI, but this often does not occur. Reviewing antibiotics in patients with new diagnoses of CDI can identify opportunities to stop unnecessary antibiotics, which improves the clinical response of CDI to treatment and reduces the risk of recurrence.
- **Treatment of culture-proven invasive infections**
 Invasive infections (e.g., blood stream infections) present good opportunities for interventions to improve antibiotic use because they are easily identified from microbiology results. The culture and susceptibility testing often provides information needed to tailor antibiotics or discontinue them due to growth of contaminants.

5.3.2.2. Antimicrobial self-revision by prescribers

This is a scheduled reassessment of the need and choice of antimicrobials by a prescriber. It entails a prescriber performing a post-prescription review of antimicrobials with regard to indication, choice of therapy, dose, route of administration, interval, duration, and/or adaption to microbiological results. This review may result in de-escalation according to guidelines, dose optimisation, IV to oral switch, change in duration, or elimination of redundant therapy, among others.

The merits of this intervention are that it:

- Directly involves prescribers of the unit in charge of patients in reviewing prescribed antimicrobial treatment.

- Promotes the use of culture and sensitivity tests to guide therapy.
- Facilitates prescriber education and maintains autonomy.
- Might earn days of treatment and relieve the AMS team of work.
- Is less resource intensive than audit and feedback.

The demerits of this intervention are:

- Opposition from prescribers and lack of hospital official policy for implementing it (policy for documentation of medicines in medical records or prescription charts).
- It may not happen if prescribers are not prompted or comfortable with making changes.

5.3.2.3. Prescriber education

All Healthcare facilities should have a programme of ongoing education for prescribers on prudent AMU. The principles of prudent antimicrobial prescribing should be included in orientation training for all new medical, nursing, laboratory, and pharmacy staff.

5.3.2.4. Antimicrobial prescribing surveillance and audit

The AMS team in each health care facility shall have a system of regular surveillance and audit of AMU employing such metrics such as DDD per 100 bed-days reported quarterly and regular point prevalence studies annually or semi-annually. These audits shall be shared with prescribers, heads of clinical services, and sub-county and county AMS governance teams.

5.3.2.5. Prescribing aids

Healthcare facilities should consider introducing antimicrobial order forms or designating a section of the prescription chart for antimicrobial prescribing, including a requirement for clinical indication and a required duration before order renewal. Order forms should distinguish between antimicrobials used for prophylaxis and those used for active therapy. Consideration should be given to having separate order forms for peri-operative antimicrobial prophylaxis.

Healthcare facilities should introduce educational aids to guide prescribers at the point of prescribing, such as:

- Clinical algorithms for the diagnosis of infection or methods to standardise documentation of treatment decisions, such as infection stamps or stickers to be included in the clinical notes.
- Where possible, ICT support for prudent AMU, including electronic patient records, computerised prescribing, and clinical decision support software.
- Computer-based surveillance to target AMS interventions, track AMR patterns, and identify health care-associated infections and treatment-related adverse events.

5.3.2.6. Streamlining or de-escalating therapy

The terms *de-escalation* and *streamlining* describe the practice of using culture results as a basis for switching from broad-spectrum or multiple antimicrobials to more narrow-spectrum or targeted therapy. It may also include changing administration from the intravenous (IV) to the oral (PO) route or discontinuing antimicrobials if infection has been ruled out.

De-escalation and streamlining may also include narrowing the antimicrobial selection when cultures are negative. For example, if a patient is receiving antimicrobial therapy for *Pseudomonas aeruginosa* and it is not identified in cultures, de-escalation to an agent without activity against *Pseudomonas aeruginosa* is usually appropriate. Also, if a patient is empirically started on vancomycin specifically for

methicillin-resistant *Staphylococcus aureus* and it has not been cultured, it would be reasonable to discontinue (or substitute) vancomycin. Other examples include changing ceftriaxone to penicillin for a susceptible *Streptococcus pneumoniae* isolate, vancomycin to cloxacillin for methicillin-susceptible *Staphylococcus aureus*, and ciprofloxacin to ampicillin for cystitis caused by a susceptible *Escherichia coli*.

Although it is often necessary to initiate a broad-spectrum antimicrobial regimen in patients with severe sepsis, continuing an overly broad regimen contributes to AMR and does not improve patient outcomes. De-escalation and stopping dual coverage (e.g., changing from combination therapy to monotherapy) based on microbial susceptibilities is supported by most guidelines and for most conditions.

De-escalation and streamlining are an important part of audit and feedback but can also be implemented as a separate stewardship intervention by systematically reviewing culture results and patients' indications for therapy.

5.3.2.7. Automatic stop orders

Automatic stop orders (ASOs) automatically apply stop dates for antimicrobial orders when the duration of therapy is not specified. An ASO can be individualised for specific antimicrobial classes, routes of administration, and/or indications.³⁰ The goal is to ensure that antimicrobials are continued no longer than necessary. ASOs encourage reassessment of the duration of therapy based on the patient's response to treatment and prescriber review of laboratory, microbiology, and diagnostic imaging results after the specified length of time.

ASOs can be individualised for specific antimicrobial classes or routes of administration (e.g., IV, oral) and/or indications. Typical orders are for five or seven days for treatment of infection and a single dose for

surgical prophylaxis, but these may vary depending on the indication and route of administration (e.g., shorter for the intravenous route to facilitate IV to PO conversion).

A clear policy and process are required that outline the criteria for applying an ASO and any exceptions (e.g., febrile neutropenia, endocarditis, prophylaxis).

Ideally, when an antimicrobial order is modified the original stop date should remain unchanged, but this is difficult to implement in practice. It would be useful if the day of therapy (e.g., “This is day 3 of 7”) is displayed prominently in the patient’s chart/electronic medical record to remind prescribers and other care providers when therapy needs to be reassessed. This information may also be incorporated into the process of care (i.e., during patient rounds). ASOs can also be incorporated into order sets (e.g., to restrict the duration of post-operative prophylaxis).

ASO policies should allow for adequate notice so that the prescriber can reassess therapy without premature discontinuation of the antimicrobial(s). The process must also ensure that the antimicrobial is not discontinued without the prescriber knowing. Approaches for informing prescribers of upcoming stop dates include use of reminders in the electronic medical record, generation of reports, and reminders from the pharmacist or other care providers.

ASOs are often most effective in the presence of robust clinical pharmacy services, where pharmacists are able to monitor and ensure the appropriate duration of therapy when antimicrobials are prescribed.

5.3.2.8. Dose optimization

Dose optimisation is the review and individualisation of antimicrobial dosing based on the characteristics of the patient, medication, and infection. Although antimicrobials are often prescribed in standard

doses for adults, more attention should be paid to individualised dosing as a stewardship initiative for improving clinical outcomes and minimising AMR.

Attention to the dose of the antimicrobial is very important when treating an infection. A dose that is too low will compromise the chances of successful treatment and increase the risk of developing resistance. A dose that is too high can increase the patient's risk of adverse effects.

Dose optimisation involves optimisation of antimicrobial dosing based on patient characteristics (e.g., weight, renal/liver function); causative organism; site of infection (e.g., central nervous system, blood); and pharmacokinetic and pharmacodynamic characteristics of the medicine (e.g., concentration or time dependent activity).

Dose optimisation is a common AMS strategy and is often integrated into the medication-review process by pharmacists. It frequently involves the reduction of doses for renally eliminated agents in patients with renal dysfunction; however, increasing doses for certain disease states (central nervous system infections, endocarditis, bone and joint infections); specific organisms (MRSA, multi-drug-resistant *Pseudomonas aeruginosa*); and obesity is also important.

Recommended doses and regimens should be incorporated into empiric treatment guidelines, clinical pathways, and predefined orders to ensure that the appropriate regimen is prescribed for specific infections.

Dosing and administration schedules that maximise the pharmacokinetic and pharmacodynamic profiles of the antimicrobial are important for optimising their effect. For example, using once daily or extended dosing of aminoglycosides instead of traditional dosing (lower doses administered two or three times daily) can improve bacterial eradication and decrease the risk of nephrotoxicity and ototoxicity.

A more advanced dose optimisation strategy involves the use of extended/prolonged or continuous infusions of beta-lactam antibiotics instead of the traditional bolus administration. This approach has been shown to improve clinical outcomes (including decreased mortality) for critically ill patients and individuals infected with more resistant organisms. This is a more labour-intensive programme to implement and in practice is often limited to academic centres and critical care units. Beta-lactam infusion programmes are of higher difficulty and lower priority than other dose-optimisation initiatives and should not be considered an essential component of this strategy.

5.3.2.9. Parenteral to oral conversion

Hospital antimicrobial prescribing guidelines should include clinical criteria and guidelines for converting parenteral antimicrobial therapy to oral therapy once the patient's condition allows. AMS teams should have a system in place for identifying patients whose antimicrobial therapy is suitable for parenteral-to-oral conversion.

5.3.2.10. Access to high-quality laboratory service

Hospitals should have access to an accredited microbiology laboratory. There should be prompt clinical liaison for critical results, such as positive sterile site cultures. The laboratory should use a standardised method for antimicrobial susceptibility testing, such as the method produced by the Clinical Laboratory Standards Institute (CLSI). The laboratory should carry out surveillance of AMR with feedback of standardised data to local prescribers.

Annual antibiograms for common pathogens or conditions (e.g., antimicrobial susceptibilities for organisms causing UTI) or for specific units or patient groups (e.g., intensive care unit), should be reviewed according to local requirements. The susceptibility data included in the annual antibiogram should be based on the first clinical isolate of a given pathogen per patient. The production and feedback of the

annual antibiogram report should be in line with the relevant CLSI guidelines. The laboratory should ensure that the correct samples from appropriate specimens are taken for the investigation of possible infections through prescriber education and direct clinical liaison.

5.3.2.11. Restrictive and interpretative laboratory reporting

Laboratories should report antimicrobial susceptibilities only where clinically indicated, and these should be restricted to agents included in the antimicrobial formulary. Where susceptibility results are reported, these should be restricted to the narrowest spectrum agents to which the organism is susceptible. Susceptibility results for broad spectrum agents should be restricted but may be made available to clinicians following appropriate clinical liaison.

Laboratories should include interpretative comments on reports to guide prescribers in deciding whether antimicrobial therapy is required and, if so, what drug to prescribe.

Laboratory results should be reported in a way that encourages prescribers to discuss the results with a microbiologist or other member of the AMS team before deciding to prescribe an antimicrobial agent.

5.3.2.12. Rapid diagnostics and inflammatory markers

Laboratories should develop, or provide access to, rapid diagnostic methods that can rapidly confirm the presence of a bacterial pathogen (e.g., polymerase chain reaction [PCR] identification of *Neisseria meningitidis* in blood or cerebrospinal fluid) or help to rule out a bacterial infection (e.g., PCR identification of respiratory viruses in children with lower respiratory tract infection). Laboratories should provide rapid testing for inflammatory markers that can help to confirm or rule out serious bacterial infection, monitor response to therapy, and guide the duration of antimicrobial therapy.

5.4. Health facility-based interventions (Levels 3 and 2)

- Ensure facilities have access to clean water and have a sanitation, hygiene, and waste management infrastructure.
- Promote training of health care workers on AMR and good antimicrobial prescribing.
- Ensure improved supply chain management to reduce use of inappropriate antimicrobials
- Avail rapid diagnostic techniques for primary health care settings.
- Promote utilisation of facility and community management of childhood illnesses that have been shown to reduce antimicrobial prescribing.
- Improve quality and safety of care using the Kenya Quality Model for Health standards.
- Monitor and survey AMC.

5.5. Community pharmacy-based interventions

Community pharmacies (CPs) have a direct role in promoting the optimal use of antimicrobial agents; reducing the transmission of infections; and educating health professionals, patients, and the public on AMS. They should enforce the fact that antimicrobials are prescription only medicines that should not be bought OTC without a valid prescription. Pharmacy professionals in CPs can support both improving clinician prescribing and educating patients and clients on why antimicrobials are only prescribed and used when needed. They can also educate patients and clients regarding complications to be aware of and on ensuring the selection of the right medication, dose, and duration. Through a CQI approach, a CP should strive to achieve the AMS elements of commitment, action, tracking and reporting, and education and expertise.

5.5.2. Commitment

Pharmacy personnel in a CP shall demonstrate dedication to and accountability for optimising antimicrobial prescribing and patient safety related to antimicrobials. This shall be achieved by:

- Displaying posters, fliers, or other forms of information about AMS.
- Appointing one pharmacy staff member to direct AMS activities within the CP.
- Including AMS-related duties in job descriptions and performance appraisal tools for pharmacy personnel.
- Using consistent messages when communicating with the public about the indications for and use of antimicrobials.
- Pursuing certification in AMS or taking AMS courses.

5.5.3. Action

The CP shall have the following interventions in place to improve antimicrobial prescribing:

- Encouraging prescribers to include the diagnosis on prescriptions to allow verification of appropriate antimicrobial, dose, and duration.
- Encouraging prescribers to include a weight on paediatric prescriptions to verify dosing.
- Suggesting alternatives when evidence-based treatment is not ordered.
- Notifying prescribers if antimicrobial appears to be redundant in spectrum coverage.
- Verifying that dose optimisation has been met.
- Verifying duration if it appears to be excessive.
- Referring clients with reported penicillin allergy with no previous testing or history of reaction inconsistent with true allergy to primary care for confirmation testing.
- Inquiring about clients' signs and symptoms and providing recommendations for OTC medications, rather than

antimicrobials, to provide relief, such as in the case of coughs and colds.

- Providing communications skills training for pharmacy personnel addressing benefits and risks of antimicrobial treatment.
- Assisting clients with management of self-limiting conditions.
- Supporting clinicians regarding managing patient expectations for antimicrobials.
- Using a script for prescriber call-backs when making prescription clarifications.
- Providing clients with printed information with specific recommendations for antimicrobial use when necessary.
- Using a standard approach for recommendations when assisting clients selecting OTC symptom relief.
- Providing recommendations to clients on when to contact a health care provider if the medication does not appear to be working or complications occur.
- Providing point of care testing and immunisations when available within the pharmacy.
- Asking every patient about vaccination status and discussing recommended vaccinations.
- Monitoring for adverse effects of antimicrobials and documenting and reporting to the PPB.
- Identifying and reporting any sub-standard, counterfeit, or poor-quality antimicrobials on the market to the PPB.

5.5.4. Tracking and reporting

A CP shall monitor at least one aspect of antimicrobial prescribing on a regular basis, including:

- Tracking and reporting improvement in number of patients reached by chosen actions for policy and practice.
- Providing feedback in the form of antimicrobial prescribing summaries to clinicians about their ordering practices, including type of antimicrobials ordered and frequency in a three- or six-month period.

- Tracking antimicrobials associated with respiratory tract infections as these account for a significant percentage of outpatient prescriptions and many are considered unnecessary.
- Tracking calls made to prescribers to record whether they adopt or reject recommendations related to antimicrobials (rate of acceptance) and sharing this information with prescribers along with best practice recommendations.
- Tracking overall antimicrobial percentage dispensed monthly.
- Determining the percentage of antimicrobials in medications dispensed per month; if a single prescriber or group is driving the numbers, notify the individual/group as appropriate.
- Determining the percentage of antimicrobial classes of concern (e.g., fluoroquinolones) of all antimicrobials dispensed per month; if a single prescriber or group is driving the numbers, notify the individual/group as appropriate.
- Calling individuals with antimicrobials dispensed 24 to 48 hours earlier to track and report on antimicrobial complications and remind clients to contact their health care providers.

5.5.5. Education and expertise

Pharmacy personnel in a CP shall provide resources to clinicians and patients on evidence-based antimicrobial prescribing.

5.5.5.1. Education to patients

- Using effective communications strategies to educate patients about when antimicrobials are and are not needed (e.g., provide information on methods to reduce symptoms if antimicrobials are not appropriate, recommend contacting primary provider if antimicrobials may be appropriate).
- Educating patients about the potential risks of antimicrobial treatment (e.g., signs and symptoms of complications when dispensing antimicrobials).

- Educating clients on serious side effects of antimicrobials, including nausea, abdominal pain, diarrhoea, CDI, allergic reactions, and other serious reactions.
- Providing information on preventive medicine and wellness initiatives (e.g., vaccinations).
- Providing patient education in multiple forms (e.g., posters, newsletters, brochures, Facebook, webpage, public presentation in the community).

5.5.5.2. Education to clinicians

- Providing face-to-face educational training.
- Providing continuing education activities for pharmacy personnel.
- Ensuring timely access to persons with expertise.

5.6. Community-based interventions

Community-targeted interventions:

- Raise awareness about the prevention of common conditions (e.g., malaria, pneumonia).
- Promote improved water, sanitation and hygiene practices.
- Advocate for appropriate AMC (e.g., completion of treatment as prescribed, proper storage practices).
- Promote follow-up of patients on treatment to enhance compliance and proper storage of antimicrobials.
- Empower the public to understand their food sources.
- Seek sustainable solutions to limit use of antimicrobials in farming while protecting farmers' livelihoods through community leaders and networks and use of incentives (e.g. premium pricing of organic produce).
- Promote community-based monitoring to track AMC.
- Promote intersectoral collaboration at the community level (e.g. agriculture, veterinary, environment, human health).

CHAPTER 6 STEPWISE APPROACH TO ESTABLISHING A STEWARDSHIP PROGRAMME AT A HEALTH CARE FACILITY

6.1. Form an antimicrobial stewardship committee

The AMS Committee should bring together health care facility stakeholders, including any personnel with an ID or pharmacy background or expertise, to keep them engaged in and updated on stewardship activities, successes, and challenges. The committee is also important for obtaining agreement and buy-in from various departments to enhance the likelihood of a successful programme. The designated focal point for stewardship activities should sit within this committee, ideally as the chair or lead.

Representation on this committee can be fundamental to the success of the AMS programme. Nurses and infection control personnel are also important to include since their involvement in stewardship activities is needed and they can provide valuable linkages to related initiatives in a facility, such as multidrug-resistant organism or health care-associated infection surveillance.

6.2. Business case development

For some Healthcare facilities, once an AMS Committee has been established, it may be prudent to identify the funding and support required to move to the next steps of implementing the stewardship programme. It is likely that a business case for funding the programme will be required in private and some public facilities. Those who control the budgets for funding initiatives like a stewardship programme may have to be persuaded of the benefits of such a scheme in the face of competing funding priorities.

In this context, the metrics that can help support a business case for a stewardship programme include:

- Reduction in length of stay for inpatients.
- No increase in intensive care unit length of stay.

- Reduced expenditure on antimicrobials.
- Reduced consumption of broad-spectrum antimicrobials.
- No increase in mortality.
- Reduced incidence of infections due to key multi-drug resistant organisms.

This business case should outline any initial and ongoing education and training requirements that might need to be funded to further develop the individuals or staff groups recruited/redeployed to stewardship activities, including attending training days, courses, or conferences.

6.3. Start with a single priority area of the AMS programme

In most Healthcare facilities, there are many areas in which AMU can be optimised but attempting to introduce change in many areas simultaneously can be difficult, especially with substantial resource constraints. It is recommended to start with a single priority or focus for the programme. The priority area would ideally be identified by reviewing existing data on AMU, if available, or by conducting a focused needs assessment or situational analysis of AMU at the facility. In the absence of data, expert opinion, such as that of the AMS Committee, should be used to identify the priority area.

Identifying the priority area should take into account existing hospital resources, such as laboratory and pharmacy capacity, which may limit addressing some priority items despite known issues. Priorities may also be focused within a specific unit or area where AMU is known to be high (e.g., an intensive care unit or operating room where perioperative prophylaxis is given) and do not need to be facility-wide to be meaningful. Initial priorities might also be facility-wide but narrowly defined in terms of their scope, such as reviewing the need for antimicrobials after 48 hours, especially when cultures are negative. Examples of priorities are:

- Reducing inappropriate use of colistin, carbapenem, or third-generation cephalosporin antimicrobials.
- Improving adherence to guidelines for empiric treatment for community-acquired pneumonia or sepsis.

- Ensuring appropriate use of antimicrobials during surgical prophylaxis.

6.4. Appropriate policies or guidelines for the priority area

To improve AMU, there should be standard treatment guidelines (STGs) to strive toward. In the absence of STGs, it becomes difficult to hold prescribers accountable for ideal use and encourage changes in practice. Facilities may use national, regional, or local STGs and modify them as needed for their facility (e.g., medicines availability, acuity of patients). STGs do not need to be overly exhaustive or based on rigorous, locally produced evidence. Facilities may choose to start with a short, targeted document for the priority area based on a simple adaptation of national guidelines to fit the local context.

6.5. Educate staff and publicise stewardship campaign

Once a priority area is chosen and policies and guidelines are in place, frontline staff may require additional education around these guidelines. Even if guidelines are already in place, a refresher training via in-service training or other educational opportunities (e.g., grand rounds) may be helpful. Educating staff should not be viewed as a single endeavour but rather an ongoing process with training repetition, as is feasible for the facility to support, to ensure that new staff; rotating staff (e.g., interns, junior doctors); and students receive education and guidelines are reinforced for previously trained personnel. Education of staff may be general or targeted depending on the priority area chosen. For example, if the priority area is around surgical prophylaxis, focusing on training surgeons, anaesthesiologists, and nurses on surgical floors would be the priority.

Publicising the stewardship campaign and alerting staff to upcoming stewardship activities around the priority topic will be critical to raise awareness of the AMS programme and gain buy in from prescribers and other health care personnel. Programmes can engage champions, such as senior surgeons, physicians, or administrators within targeted groups, to lead education and publicity efforts. This might include

posters, text messages, posts on social media, or other modalities already in use in a facility to promote messaging.

6.6. Implement stewardship activities targeted at the priority

The designated stewardship leader, with the buy-in of the committee, should choose up to three activities targeted at the priority area, which will comprise the core of the AMS programme. As a general rule, starting with fewer activities and doing them well is preferable to implementing more activities that can be difficult to execute simultaneously.

Given that there are many types of stewardship activities with a range of complexity and resource requirements, thought should be given to what is realistic to achieve in a facility and which activities will most likely have the desired impact on the priority area.

CHAPTER 7 || POTENTIAL PITFALLS AND MITIGATION

Table 13: Potential pitfalls in antimicrobial stewardship and mitigation

| Pitfall Identified | Proposed Mitigation |
|---|--|
| <p>1 Insufficient resources to implement AMS programmes, including IT, human, and financial resources</p> | <ul style="list-style-type: none"> • Undertake resources mapping, conduct resource mobilisation, and identify and engage development and technical partners in the field of AMR • Lobby county governments to allocate sufficient resources for AMS • Make economic case for AMS to policy makers through sustained lobbying and advocacy |
| <p>2 Weak pharmaceutical information management systems</p> | <ul style="list-style-type: none"> • Provide support to strengthen pharmaceutical information management systems at all levels of AMC and use and establish electronic pharmaceutical/health records management systems, which can be implemented in the context of pharmaceutical systems strengthening programmes |
| <p>3 Lack of national baseline data on AMU and AMC</p> | <ul style="list-style-type: none"> • Conduct baseline surveys on AMU and AMC • Conduct PPS in the context of longitudinal studies to generate national data on status of AMU in Kenya |
| <p>4 Lack of or inadequate operational research</p> | <ul style="list-style-type: none"> • Support operational research, entry level of researches at MTCs at national, sub-national, and facility levels • Operational research can also be conducted and reported by AMS Committees at Healthcare facilities |

| Pitfall Identified | Proposed Mitigation |
|---|--|
| <p>5 Weak documentation at facility levels</p> | <ul style="list-style-type: none"> • Undertake training, capacity building, and mentorship of health care workers in the area of AMS; establish twinning programmes by pairing a facility that is running a successful AMS programme with one that does not have a successful AMS programme • Conduct more frequent health facility audits and emphasise linking good documentation to quality of patient care |
| <p>6 Lack of capacity for optimal use of laboratory services/NPHLS and laboratory network (gene resistance patterns, antimicrobial sensitivity testing)</p> | <ul style="list-style-type: none"> • Implement capacity building, mentorship, and training programmes for health care workers on microbiology and provide continuous updates on new methods and techniques in microbiology • Procurement and deployment of new diagnostic laboratory techniques (e.g., PCR for <i>Neisseria meningitidis</i>, C-reactive proteins) |
| <p>7 Inadequate regulation of pharmacy practice, inadequate restriction of use of some antimicrobials, inadequate restriction of imports of some antimicrobials, inadequate reviews of schedules of antimicrobials agents</p> | <ul style="list-style-type: none"> • Finalise the scheduling and rescheduling of antimicrobials, as per the AWaRe categorisation; implement colour-coded prescriptions • Train and deploy AMU auditors and create partnerships with county and sub-county pharmacists in the area of routine audits of AMU and AMC • Enforcement of restrictions on OTC issuance and dispensing of antimicrobial agents |
| <p>8 Lack of awareness in the community on AMR</p> | <ul style="list-style-type: none"> • Implement awareness, sensitisation, and social behaviour change programmes on AMR at the community level • These include media talk shows, social media, training of media on AMR, advocacy |

| Pitfall Identified | Proposed Mitigation |
|--|---|
| | <p>at community opinion leaders, CHVs, and CHAs</p> |
| <p>9 Lack of/ineffective quality of clinical care audits/implementation of findings and recommendations</p> | <ul style="list-style-type: none"> • Strengthen quality of clinical care audits and support implementation of recommendations • Designating quality improvement staff in hospitals to support optimal use of antimicrobials |
| <p>10 Lack of standardised treatment protocols in the private sector</p> | <ul style="list-style-type: none"> • Develop and implement standard treatment protocols and facility-specific treatment guidelines based on national guidelines, local antimicrobial sensitivity testing data, and formulary options and align them to international best clinical practice guidelines • MTC should be involved • Link treatment protocol adherence to NHIF reimbursement |
| <p>11 Inadequate and slow uptake of IT platforms and innovation in AMS</p> | <ul style="list-style-type: none"> • Embed IT tools and protocols at the point of care (e.g., immediate access to facility-specific guidelines at point of prescribing) • Implement clinical decision support systems for antibiotic use, creating prompts for action to review antibiotic use • Employ IT to collect and utilise consumption and use data on antimicrobials • Develop and deploy antibiotic treatment guides through mobile phone applications |

| Pitfall Identified | Proposed Mitigation |
|--|---|
| <p>12 Lack of hospital-specific antibiograms</p> | <ul style="list-style-type: none"> • Develop hospital-specific antibiograms that can be applied for decision making |
| <p>13 Lack of clear coordination of interventions at facility level</p> | <ul style="list-style-type: none"> • Map out AMR interventions at hospital/facility level; prioritise interventions with high impact based on the needs of the hospital to leverage limited resources • Avoid implementing too many interventions simultaneously and avoid duplication • Ensure buy-in by top management level for easier coordination and improved teamwork |
| <p>14 Ineffective M&E systems for AMS</p> | <ul style="list-style-type: none"> • Delegate an AMS champion (or AMS-lead delegated from the MTC) at the facility level • Develop M&E indicators at the facility level and review indicators continuously • Monitor and evaluate effectiveness of AMS programmes, systems, and tools (e.g., tracking clinical outcomes to measure impact of interventions to improve antibiotic use) • Monitor resistance at the patient level (e.g., how many develop resistant super-infections, those under influence of steward interventions) and aim for continuous improvement • Track health care-acquired infections at the facility level • Establish a prescriber-feedback channel to counsel nonadherent prescribers |

| Pitfall Identified | Proposed Mitigation |
|---|--|
| <p>15 Lack of pharmacy-led stewardship programmes</p> | <ul style="list-style-type: none"> • Get buy-in/support from facility administration for establishing pharmacy-led stewardship programmes • Build capacity of pharmacy personnel, including continuing professional development • Implement pharmacy-led stewardship programmes |
| <p>16 Weak feedback mechanisms to health care workers on AMS gains and updates</p> | <ul style="list-style-type: none"> • Implement a communication strategy on AMS • Direct prescriber feedback to prescribers and other health care workers. • Annual publications on facility-specific antimicrobial susceptibility data • Issue quarterly AMS bulletins |

CHAPTER 8 **MONITORING AND EVALUATION OF ANTIMICROBIAL STEWARDSHIP PROGRAMMES**

Data play an important role in assessing AMS interventions by identifying the problems and assessing the benefits of the interventions, but keep in mind that in some situations qualitative improvement can be achieved even in the absence of data. This may especially be true if the quality of provided care is far from optimal, as is the case with regard to the use of antimicrobials in many settings. However, in the mid- to long-term perspective, efficient prioritisation of interventions and resource allocation for AMS requires data to identify the key problems and demonstrate the impact of specific interventions. Indicators of AMU are an essential part of any AMS strategy.

Facilities are encouraged to select the metrics most relevant for and most feasible in their local setting, since assessing all indicators is unrealistic. The resources required for assessing the indicators vary depending on the health care setting and the available infrastructure. However, given the complexity of AMU, a single indicator will probably not be sufficient.

AMS measurement and assessment systems should be part of existing monitoring systems and be linked to the measurement of performance in a health care facility. AMS M&E measurements should be embedded into the AMS programme and, as much as possible, into the existing workflows to ensure effectiveness, sustainability, acceptance, and minimal disruption of day-to-day service delivery.

Different categories of AMS measurements need to be put in place, including:

8.1. Structure measures

Structure measures for AMS programmes ask:

- Are the right elements in place?
- Are the resources, lines of reporting, and policies available?

These measures should provide evidence of developing, implementing, and regularly reviewing the effectiveness of AMS systems. They help to determine whether the appropriate governance, workforce, and processes, such as working committees, formularies, and guidelines, are in place and maintained. Self-assessment tools need to be developed for different levels and contexts to guide structure assessments.

8.2. Process measures

Process measures determine whether policies and processes are being followed correctly. They play a role in answering the questions:

- Are our systems performing as planned?
- Are they effective?

These measures should be instituted as regular audits and periodically reported back to prescribers and other clinicians. They can help maintain appropriate medicine use. Development of process measures should involve multidisciplinary teams to ensure appropriateness and ownership. These measures may include:

- Rates of adherence to guidelines.
- Appropriateness and timeliness of therapy for a given infection.
- Rates of prescribing concordant with susceptibility reporting.

8.3. Outcome measures

Outcome measures aim to assess the effect of AMS in terms of whether patient outcomes have improved, adverse events have decreased, and infections caused by resistant pathogens have decreased. These measures ask the question, “What is the result of our AMS interventions?” It is also important to measure economic outcomes to ensure continued support for AMS initiatives by management.

Given that there are several factors that can contribute to patient outcomes, it is not often possible to ascribe changes in patient outcome solely to AMS programmes. However, process measures that can reliably be related to improvements in outcomes may be used as surrogates for outcome measures. Examples of outcome measures include:

- Infection-related mortality rates.
- Length of hospital stay.
- Time to respond to treatment.
- Changes in antimicrobial treatment costs.
- Antimicrobial acquisition costs.

8.4. Balancing measures

Balancing measures relate to whether changes as a result of AMS programmes might cause new problems. They ask the question, “Are the changes causing new problems?”

These measures look at potential unintended consequences of AMS interventions such as undertreatment of infections and poorer clinical outcomes due to antibiotic under prescribing. There should also be vigilance over the creation of new selective pressures on microbial flora that cause potential new clinical problems, such as the emergence of new multidrug-resistant strains or the re-emergence of infections that were previously uncommon.

Balancing measures include:

- Incidence of adverse drug events (e.g., cardiac toxicity, renal impairment).
- Incidence of allergic reactions.
- Infection-related mortality.
- Infection-related readmission rates.
- Rates of surgical site infection.

8.5. Qualitative and other related measures of AMS programme activity

These measures can be used to inform the AMS team about how well the programme is operating and to identify further areas for improvement.

- User acceptance can be measured directly through surveys or questionnaires for clinicians; questions might cover awareness of the programme, effectiveness of the interface with the AMS team, and the degree to which the AMS team's advice was considered useful.
- Surveys and questionnaires can also provide opportunities for the AMS team to get feedback that can be used to improve the AMS programme. They can also help to assess the perceptions and attitudes of prescribers about AMR.
- Surveys should also be conducted to assess consumer awareness and attitudes toward AMS programme interventions. These can help in guiding the approach to be taken in ensuring consumer involvement in AMS activities.
- Ongoing surveillance of AMU is essential to measure the effect of stewardship interventions.
- Regular, small quality improvement audits can help to drive changes in prescribing.
- The measurement and evaluation of AMS initiatives should be facilitated using standardised formats and IT systems for collecting, analysing, and reporting data.
- Timely feedback and reporting to clinicians and health service managers is a key component of effective AMS.
- M&E measures should not be focused on judging whether data meet a compliance target but on determining whether the AMS changes made to improve practice are effective and to what degree.

REFERENCES

1. Barker et al. Social determinants of antibiotic misuse: a qualitative study of community members in Haryana, India. *BMC Public Health* (2017) 17:333.
2. Kalungia et al. Non-prescription sale and dispensing of antibiotics in community pharmacie in Zambia. *Expert Review of Anti-Infective Therapy*, 2016. Vol. 14, No. 12, 1215–1223.
3. O’Neill et al. Review on antimicrobial resistance. Tackling drug resistance infections globally. Available at: <https://amr-review.org/>.
4. Okeke IN, Aboderin OA, Byarugaba DK, et al. Growing problem of multidrug-resistant enteric pathogens in Africa. *Emerg Infect Dis.* 2007;13(11):1640–1646.
5. UNAS, CDDEP, GARP-Uganda, Mpairwe Y, Wamala S. Antimicrobial Resistance in Uganda: Situation Analysis and Recommendations: Uganda National Academy of Sciences; Center for Disease Dynamics, Economics & Policy:107; 2015.
6. Ampaire L, Muhindo A, Orikiran P, et al. A review of antimicrobial resistance in East Africa. *Afr J Lab Med*; 5(1); 2016.
7. Okoth C, Opanga S, Oluka M, et al. Point prevalence survey of antibiotic use and resistance at a referral hospital in Kenya: findings and implications. *Hospital Practice* Vol 46(3); 2018.
8. Momanyi L, Opanga S, Nyamu D, et al. Antibiotic prescribing patterns at a leading referral hospital in Kenya: a point prevalence survey. *Journal of Research in Pharmacy Practice*, 2019.
9. Mukokinya MM, Opanga S, Oluka M, Godman B. Dispensing of antimicrobials in Kenya: a cross sectional pilot study and its implications. *Journal of Research in Pharmacy Practice*; 7 (2): 77, 2018.
10. Miller-Petrie M, et al. Socioeconomics, antimicrobial use and antimicrobial resistance. *Economics and Innovation*; 2017. Available at:

- antimicrobial-use-and-antimicrobial-resistance.
11. Nowak MA, et al. Clinical and economic outcomes of a prospective antimicrobial stewardship program. *American Journal of Health-System Pharmacy*, 69(17): p. 1500–1508; 2012.
 12. National OPAT Conference 2018. British Society for Antimicrobial Chemotherapy. Available at: www.bsac.org.uk.
 13. Impact of Antibiotic Stewardship Program Interventions on Costs. Available at: <https://www.cdc.gov/antibiotic-use/healthcare/evidence/asp-int-costs.htm>.
 14. Karanika S, Paudel S, Grigoras C, Kalbasi A, Mylonakis E. Systematic review and meta-analysis of clinical and economic outcomes from the implementation of hospital-based antimicrobial stewardship programs. *Antimicrob Agents Chemother* 60:4840–4852; 2012. Available at: <http://www.doi:10.1128/AAC.00825-16>.
 15. Mendelson M, Whitelaw A, Nicol M, Brink A. Wake up South Africa! The antimicrobial ‘horse’ has bolted S Africa *Med J*, 102; 607–608; 2012.
 16. Antimicrobial resistance communication activities in South East Asia. *BMJ* 358:j2742; 2017.
 17. Park S, Soumerai SB, Adams AS, et al. Antimicrobial use following a Korean national policy to prohibit medication dispensing by physicians. *Health Policy Plan*, 20: 302–309; 2005.
 18. Chou YJ, Yip WC, Lee CH, Huang N, Sun YP, Chang HJ, Impact of separating drug prescribing and dispensing on provider behavior: Taiwan's experience *Health Policy Plan*, 18: 316–329; 2003.
 19. Bavestrello FL, Cabello MA. Community antimicrobial consumption in Chile, 2000–2008. *Rev Chilena Infectol*, 28; 107–112; 2011.
 20. WHO, Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new

- antibiotics. Available at:
https://www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf?ua=1.
21. Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP, et al. Infectious Diseases Society of America; Society for Healthcare Epidemiology of America. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis*. 2007;44(2):159–77. Available at: <http://cid.oxfordjournals.org/content/44/2/159.long>.
 22. Pharmacists Help Drive Antimicrobial Stewardship Programs. Available at: <https://www.infectioncontroltoday.com/stewardship/pharmacists-help-drive-antimicrobial-stewardship-programs>.
 23. Antimicrobial stewardship. From principles to practice. British society for antimicrobial chemotherapy. 2018.
 24. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an Antimicrobial Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016.
 25. MacDougall C, Polk R. Antimicrobial stewardship programs in health care systems. *Clinical Microbiology Reviews*; 18(4):638–656; 2005.
 26. World Health Organization. Global Framework for development stewardship to combat antimicrobial resistance; 2017.
 27. Ndihokubwayo JB, et al. Antimicrobial resistance in the African Region: Issues, challenges, and actions proposed. Available at: <https://apps.who.int>.
 28. Dellit TH, Owens RC, McGowan JE Jr, et al. IDSA and SHEA Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship. *Clin. Infect. Dis*. 44:159–77; 2007.

29. Practical Guide to Antimicrobial Stewardship in Hospitals. Available at: <http://bsac.org.uk/wp-content/uploads/2013/07/Stewardship-Booklet-Practical-Guide-to-Antimicrobial-Stewardship-in-Hospitals.pdf>.
30. Antimicrobial stewardship strategy. Automatic stop orders. Available at: https://www.publichealthontario.ca/apps/asp-strategies/data/pdf/ASP_Strategy_Automatic_Stop_Orders.pdf.
31. Barza M, Ioannidis JP, Cappelleri JC, Lau J. Single or multiple daily doses of aminoglycosides: a meta-analysis. *BMJ*, 312(7027):338–45; 1996.
32. Antimicrobial resistance and primary health care. WHO/HIS/SDS/2018.57
33. Antimicrobial resistance. Available at: <http://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>.
34. Overcoming gaps in R&D on AMR meeting, Brasilia, 26-27th March 2015. High-level Technical Meeting. WHO, OIE, Civil Society Organizations, Government of Brazil and other governments.
35. Antimicrobial stewardship guidelines. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5436405/>.
36. Cockburn R, Newton PN, Agyarko EK, et al. The global threat of counterfeit drugs: why industry and governments must communicate the dangers. *PLoS Med*. 2(4):e100; 2005. Available at: <http://dx.doi.org/10.1371/journal.pmed.0020100>.
37. Murray CJL, Ezzati M, Flaxman AD, et al. GBD 2010: a multi-investigator collaboration for global comparative descriptive epidemiology. *Lancet*. 380(9859):2055–2058; 2012. Available at: [http://dx.doi.org/10.1016/S0140-6736\(12\)62134-5](http://dx.doi.org/10.1016/S0140-6736(12)62134-5).
38. British Society of Antimicrobial Chemotherapy: Antimicrobial stewardship from principal to practice. Available at: www.bsac.org.uk.
39. Huttner B, Goossens H, Verheij T, Harbarth S. Characteristics and outcomes of public campaigns aimed at improving the

- use of antimicrobials in outpatients in high-income countries. *Lancet Infect Dis*, 10: 17–31; 2010.
40. Sabuncu E, David J, Bernede-Bauduin C, et al. Significant reduction of antimicrobial use in the community after a nationwide campaign in France, 2002–2007. *PLoS Med*, 6: p. e1000084; 2009.
 41. Wirtz VJ, Herrera-Patino JJ, Santa-Ana-Tellez Y, et al. Analyzing policy interventions to prohibit over-the-counter antimicrobial sales in four Latin American countries. *Trop Med Int Health*, 18: 665–673; 2013.
 42. Global Framework for Development & Stewardship to Combat Antimicrobial Resistance. Available at: http://www.who.int/phi/implementation/research/WHA_BackgroundPaper-AGlobalFrameworkDevelopmentStewardship.pdf.
 43. Leung E,^a Weil DE.^a The WHO policy package to combat antimicrobial resistance. *Bull World Health Organ*. 89(5): 390–392; 2011.
 44. Duguid M, Cruckshank M. Antimicrobial stewardship in Australian hospital 2011. Available at: <https://www.safetyandquality.gov.au>.
 45. South African NAP strategy 2014–2024. Available at: www.health.gov.za.
 46. Shortages and access to antimicrobials. Available at: https://accesstomedicinefoundation.org/media/atmf/Antibiotic-Shortages-Stockouts-and-Scarcity_Access-to-Medicine-Foundation_31-May-2018.pdf
 47. McGowan JE. Antimicrobial stewardship: the state of the art in 2011 – focus on outcome and methods. *Infect Control Hosp Epidemiol* 2012;33(4):331–7.
 48. Slain D, Sarwari AR, Petros KO, McKnight RL, Sager RB, Mullett CJ, et al. Impact of a multimodal antimicrobial stewardship program on *Pseudomonas aeruginosa* susceptibility and antimicrobial use in the intensive care unit setting. *Crit Care Res and Prac* 2011;2011:416–26.

49. Bell S, Davey P, Nathwani D, Marwick C, Vadiveloo T, Sneddon J, et al. Risk of AKI with Gentamicin as surgical prophylaxis. *J Am Soc Nephrol* 2014;25(11):2625–32.
50. Goff DA. Antimicrobial stewardship: bridging the gap between quality care and cost. *Curr Opin Infect Dis* 2011;24(Suppl 1):11–20.
51. Nathwani D, Sneddon J, Malcolm W, Wiuff C, Patton A, Hurding S, et al. Scottish Antimicrobial Prescribing Group (SAPG): development and impact of the Scottish National Antimicrobial Stewardship Programme. *Int J Antimicrob Agents* 2011;38(1):16–26.
52. Australian Commission on Safety and Quality in Healthcare, 2018. Antimicrobial Stewardship in Australian Health Care 2018.

ANNEX 1: List of reviewers

| | |
|------------------------|---|
| Dr. Andrew Thaiyah | USAID, Kenya/East Africa |
| Dr. Anish Okeyo | Thika Level 5 Hospital |
| Dr. Bernadine Lusweti | Thika Level 5 Hospital |
| Dr. Caroline Wafula | Jaramogi Oginga Odinga Teaching and Referral Hospital |
| Dr. Daniella Munene | Pharmaceutical Society of Kenya |
| Dr. Gloria Kenyatta | Machakos Level 5 Hospital |
| Dr. Irene Mramba | Coast General Hospital |
| Dr. Irene Muchoki | Nairobi County |
| Dr. Jaimini Gohil | Aga Khan University Hospital |
| Dr. Joel Mwova | County Government of Machakos |
| Dr. Joseph Mukoko | USAID MTAPS Program |
| Dr. Joy Mugambi | Kenya Medical Association |
| Dr. Kiplangat Sigei | Biomerieux |
| Dr. Lucy Ochola | Machakos Level 5 Hospital |
| Dr. Marion Ong'ayo | Mbagathi County Hospital |
| Dr. Mary Alubisia | Nyeri County Referral Hospital |
| Dr. Mirfin Mpundu | ReAct Africa / Ecumenical Pharmaceutical Network |
| Dr. Nath Arwa | Aga Khan University Hospital |
| Dr. Ndinda Kusu | USAID MTaPS Program |
| Dr. Norah Maore | Ministry of Health, Nairobi County |
| Dr. Oscar Agoro | County Government of Nyeri |
| Dr. Yaakub Ahmed | Coast General Hospital |
| Dr. Zaheer Bagha | Coast General Hospital |
| Ms. Doris Bota | USAID MTaPS Program |
| Ms. Felister Kiberenge | Ministry of Health |

Mr. Manaseh Bocha

Clinical Officers Council

Ms. Susan Githii

National Public Health Laboratory

Ms. Veronica Kamau

Ministry of Health

ANNEX 2: Checklist for antimicrobial stewardship programme in hospitals

| Antimicrobial Stewardship Component | Yes/No |
|---|--------|
| A. Leadership Support | |
| 1. Does your facility have support from leadership for efforts to improve antimicrobial use (antimicrobial stewardship), such as a dedicated budget? | |
| 2. Is this support formal and documented? | |
| 3. Does it receive any budgeted financial support from the hospital management/county for antimicrobial stewardship (AMS) activities (e.g., support for salary, training, or IT support)? | |
| B. Accountability | |
| 4. Is there a physician leader responsible for programme outcomes of stewardship activities at your facility? | |
| C. Medicines Expertise | |
| 5. Is there a pharmacist/pharmaceutical technologist leader responsible for programme outcomes of stewardship activities at your facility? | |
| Key support for the antimicrobial stewardship programme | |
| 6. Do any of the staff below work with the stewardship leaders to improve antimicrobial use? | |
| a) Clinicians | |
| b) Infection Prevention and Control | |
| c) Quality Improvement | |
| d) Microbiology (Laboratory) | |

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| e) Information Technology | |
| f) Nursing | |
| g) Other (Specify) | |
| D. Actions to Improve Optimal Antimicrobial Use | |
| Core Interventions | |
| 7. Does your facility have a policy that requires prescribers to document in the medical record or during order entry full name, dose, route, frequency, duration, and indication for all antimicrobial prescriptions? | |
| 8. Has your facility adopted prospective audits of antimicrobial use with direct interaction and feedback to prescribers, performed by either an infectious diseases physician or a clinical pharmacist with infectious diseases training? | |
| 9. Has your facility adopted formulary restriction and preauthorisation for antimicrobials? | |
| Supplemental Interventions <i>Are the following actions to improve antimicrobial prescribing conducted in your facility?</i> | |
| 10. Training on guidelines | Pre-service (induction), in-service, or informal trainings or workshops to educate health care workers on guidelines to ensure optimal use of antimicrobials to treat common infections (e.g., community-acquired pneumonia, urinary tract infection, skin and soft tissue infections, surgical prophylaxis) |

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| 11. Ward (antimicrobial) rounds | Rounds held on a regular basis to review and discuss antimicrobial choices and ensure accordance with best practice guidelines | |
| 12. Prescription alerts | Alerts to clinicians where prescriptions may be overlapping or duplicative (e.g., overlapping anaerobic activity) | |
| 13. Prior authorisation | A requirement that clinicians must get approval before select antibiotics will be dispensed for patient use | |
| 14. Antibiotic restriction | A blanket rule that clinicians are unable to prescribe certain antibiotics to certain classes of patients | |
| 15. Automatic stop order | Antibiotics are stopped automatically after a predefined time period according to indication (e.g., 24 hours for surgical prophylaxis, 5 days for community-acquired pneumonia) regardless of physician order | |
| 16. Automatic changes | An aspect of the original prescription is routinely changed, usually without requiring a new clinician order (e.g., IV to PO fluoroquinolones) | |
| 17. Selective laboratory reporting | Laboratory reports a limited number of antibiotics for susceptibility results as | |

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| | opposed to all antibiotics tested | |
| 18. Cascade laboratory reporting | Laboratory reports susceptibility testing to second-line/expensive antibiotics only if organism susceptibility testing meets certain criteria (e.g., resistant to first-line antibiotics) | |
| 19. Antibiotic timeout | Defined, regular prompts to the clinician to re-evaluate antibiotic choices (e.g., at 48 hours a clinician is prompted to review any empiric IV antibiotic therapy) | |
| 20. Antibiotic reminder | Prompts to the clinician that are tied to a particular prescription in real time (e.g., when a clinician chooses to order IV quinolones, the clinician is asked if patient can take PO) | |
| 21. Dose adjustments | Dose adjustments in cases of organ dysfunction | |
| 22. Dose optimisation | Dose optimisation (pharmacokinetics/pharmacodynamics) to optimise the treatment of organisms with reduced susceptibility | |
| 23. Does your facility have facility-specific treatment recommendations based on national guidelines and local susceptibility to assist with antimicrobial selection for the following common clinical conditions? | | |
| a) Urinary tract infections | | |

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| b) Community-acquired respiratory tract infections | |
| c) Skin and soft tissue infections | |
| d) Blood stream infections | |
| e) Surgical antimicrobial prophylaxis | |
| f) Acute pharyngitis | |
| g) Acute infectious diarrhoea | |
| h) Ventilator-associated pneumonia | |
| i) Acute otitis media | |
| j) Other (Specify) | |
| E. Tracking: Monitoring Antimicrobial Prescribing, Use, and Resistance | |
| Process measures | |
| 24. Does your stewardship programme monitor adherence to a documentation policy (dose, duration, and indication)? | |
| 25. Does your stewardship programme monitor adherence to facility-specific treatment recommendations/guidelines? | |
| 26. Does your stewardship programme monitor compliance with one or more of the specific interventions in place? | |
| Antibiotic use and outcome measures | |
| 27. Does your facility track rates of selected infections? | |
| 28. Does your facility produce an antibiogram report? (An antibiogram is an overall profile of antimicrobial | |

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| <p><i>susceptibility testing results of a specific microorganism to a battery of antimicrobial medicines.)</i></p> | |
| <p>29. Does your facility monitor antimicrobial use (consumption) by one of the following metrics?</p> | |
| <p>a) Counts of antibiotic(s) administered to patients per day (Days of Therapy; DOT)?</p> | |
| <p>b) Number of grams of antibiotics used (Defined Daily Dose; DDD)?</p> | |
| <p>c) Direct expenditure for antibiotics (purchasing costs)?</p> | |
| <p>G. Reporting Information to Staff on Improving Antibiotic Use and Resistance</p> | |
| <p>30. Does your stewardship programme share facility-specific reports on antimicrobial use with prescribers?</p> | |
| <p>31. If an antibiogram is produced, is it distributed to prescribers at your facility?</p> | |
| <p>32. Do prescribers ever receive direct, personalised communication about how they can improve their antimicrobial prescribing?</p> | |
| <p>H. Education</p> | |
| <p>33. Does your stewardship programme provide education to clinicians and other relevant staff on improving antimicrobial prescribing?</p> | |

ANNEX 3: Checklist for antimicrobial stewardship programme in community pharmacy

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|---|--------|
| A. Commitment In which of the following ways does your pharmacy demonstrate dedication to and accountability for optimising antimicrobial prescribing and patient safety related to antimicrobials? | Yes/No |
| 1. Displaying posters, fliers, or other forms of information about antimicrobial stewardship. | |
| 2. Appointing one pharmacy personnel to direct antimicrobial stewardship activities within the CP. | |
| 3. Including antimicrobial stewardship-related duties in job descriptions and performance appraisals tools for pharmacy personnel. | |
| 4. Using consistent messages when communicating with the public about the indications for and use of antimicrobials. | |
| 5. Pursuing certification in antimicrobial stewardship or taking antimicrobial stewardship courses. | |
| 6. Other (Specify) | |
| B. Action Which of the following interventions are in place to improve antimicrobial prescribing? | |
| 1. Encouraging prescribers to include diagnosis on prescriptions to allow verification of appropriate antimicrobial, dose, and duration. | |
| 2. Encouraging prescribers to include weight on paediatric prescriptions to verify dosing. | |
| 3. Suggesting alternatives when evidence-based treatment is not ordered. | |

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| 4. | Notifying prescribers if antimicrobial appears to be redundant in spectrum coverage. | |
| 5. | Verifying that dose optimisation has been met. | |
| 6. | Verifying duration if it appears to be excessive. | |
| 7. | Referring clients with reported penicillin allergy with no previous testing or history of reaction inconsistent with true allergy to primary care for confirmation testing. | |
| 8. | Inquiring about clients' signs and symptoms and providing recommendations on over-the-counter medications to provide relief. | |
| 9. | Providing communications skills training for pharmacy personnel addressing benefits and risks of antimicrobial treatment. | |
| 10. | Assisting clients with management of self-limiting conditions. | |
| 11. | Supporting clinicians regarding managing patient expectations for antimicrobials. | |
| 12. | Using a script for prescriber callbacks when making prescription clarifications. | |
| 13. | Providing clients with printed information with specific recommendations for antimicrobial use when necessary. | |
| 14. | Using a standard approach for recommendations when assisting clients selecting over-the-counter symptom relief. | |
| 15. | Providing recommendations to clients on when to contact a health care provider if the medication does not appear to be working or complications occur. | |
| 16. | Providing point of care testing when available within the pharmacy. | |
| 17. | Providing immunisations when available within the pharmacy. | |

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| <p>18. Asking every patient about vaccination status and discussing recommended vaccinations.</p> | |
| <p>C. Tracking and Reporting Which of the following aspects of antimicrobial prescribing are monitored on a regular basis?</p> | |
| <p>1. Tracking and reporting improvement in number of patients reached by chosen actions for policy and practice.</p> | |
| <p>2. Providing feedback in the form of antimicrobial prescribing summaries to clinicians about their ordering practices (e.g., type of antimicrobials ordered and frequency in a three- or six-month period).</p> | |
| <p>3. Tracking antimicrobials associated with respiratory tract infections as these account for a significant percentage of outpatient prescriptions and many are considered unnecessary.</p> | |
| <p>4. Tracking calls made to prescribers to record whether they adopt or reject recommendations related to antimicrobials (rate of acceptance) and sharing this information with prescribers along with best practice recommendations.</p> | |
| <p>5. Tracking overall antimicrobial percentage dispensed monthly.</p> | |
| <p>6. Determining the percentage of antimicrobials out of all medications dispensed per month; if a single prescriber or group is driving the numbers, notify the individual/group as appropriate.</p> | |
| <p>7. Determining the percentage of antimicrobial classes of concern (e.g., fluoroquinolones) of all antimicrobials dispensed per month; if a single prescriber or group is driving the numbers, notify the individual/group as appropriate.</p> | |
| <p>8. Calling back individuals with antimicrobials dispensed 24 to 48 hours earlier to track and report antimicrobial complications and ask clients to contact their health care providers if needed.</p> | |

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| <p>D. Education and Expertise Provision of resources to clinicians and patients on evidence-based antimicrobial prescribing</p> | |
| <p>Education to clinicians</p> | |
| <p>1. Providing face-to-face educational training.</p> | |
| <p>2. Providing continuing education activities for pharmacy personnel.</p> | |
| <p>3. Ensuring timely access to persons with expertise.</p> | |
| <p>Education to patients</p> | |
| <p>1. Using effective communications strategies to educate patients about when antimicrobials are and are not needed (e.g., providing information on methods to reduce symptoms if antimicrobials are not appropriate, recommending contacting primary provider if antimicrobials may be appropriate).</p> | |
| <p>2. Education on the potential risks of antimicrobial treatment (e.g., providing consistent customer education on signs and symptoms of complications when dispensing antimicrobials).</p> | |
| <p>3. Educating clients on serious side effects of antimicrobials, including nausea, abdominal pain, diarrhoea, CDI, allergic reactions, and other serious reactions.</p> | |
| <p>4. Providing information on preventive medicine and wellness initiatives (e.g., vaccinations).</p> | |
| <p>5. Providing patient education in multiple forms (e.g., posters, newsletters, brochures, Facebook, webpage, public presentations in the community).</p> | |

ANNEX 4

AWaRe classification of antibiotics

| Access Group | |
|---|---|
| <p>This group includes antibiotics and antibiotic classes that have activity against a wide range of commonly encountered susceptible pathogens while showing lower resistance potential than antibiotics in Watch and Reserve groups.</p> <p>Access antibiotics should be widely available, affordable and quality assured to improve access and promote appropriate use. Selected Access group antibiotics (shown here) are included on the WHO EML as essential first-choice or second-choice empirical treatment options for specific infectious syndromes.</p> | <ul style="list-style-type: none"> Amikacin Amoxicillin Amoxicillin + clavulanic acid Ampicillin Azithromycin Benzathine penicillin Benzyl penicillin Cefazolin Cefixime Ceftriaxone Doxycycline Flucloxacillin Gentamicin Metronidazole Nitrofurantoin Phenoxymethylpenicillin Tinidazole |
| Watch Group | |
| <p>This group includes antibiotics and antibiotic classes that have higher resistance potential and includes most of the highest priority agents</p> | <ul style="list-style-type: none"> Ceftazidime Ciprofloxacin Clarithromycin Clindamycin Cotrimoxazole |

among the Critically Important Antimicrobials for Human Medicine and/or antibiotics that are at relatively high risk of selection of bacterial resistance.

Watch group antibiotics should be prioritized as key targets of national and local stewardship programmes and monitoring. Selected Watch group antibiotics (shown here) are included on the WHO EML as essential first-choice or second-choice empirical treatment options for a limited number of specific infectious syndromes.

(Sulfamethoxazole/Trimethoprim)
Piperacillin + tazobactam

Reserve Group

This group includes antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multidrug-resistant organisms and treated as “last-resort” options. Their use should be tailored to highly specific patients and settings when all alternatives have failed or are

Colistin
Ertapenem
Fosfomycin
Linezolid
Meropenem
Polymyxin B
Teicoplanin
Tigecycline
Vancomycin

not suitable. They could be protected and prioritized as key targets of national and international stewardship programmes, involving monitoring and utilization reporting, to preserve their effectiveness.

Selected Reserve group antibiotics (shown here) are included on the WHO EML when they have a favourable risk-benefit profile and proven activity against “Critical Priority” or “High Priority” pathogens identified by the WHO Priority Pathogens List, notably carbapenem-resistant Enterobacteriaceae.

**Annex 5
Implementation Plan Template
Workplan for Implementation of Components of Antimicrobial Stewardship Program**

| Objective | Activities | Expected Outcome | Data Evaluation and Measurement | Timeframe for Completion | Person/ Area Responsible |
|-----------|------------|------------------|---------------------------------|--------------------------|--------------------------|
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